SIR ALEXANDER FLEMING, DISCOVERER OF PENICILLIN, EXAMINES A MOULD

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The Romance of

MEDICAL SCIENCE

BY

PATRICK PRINGLE

WITH A FOREWORD BY

ALEXANDER FRANKLIN

M.B. Ch.B.(Edin.)

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TO

MY OLD COMRADES

OF

No. 12 GENERAL HOSPITAL
M.E.F.

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FOREWORD

THE vast strides that medical science has taken in the last few years have captured the imagination of us all. Seldom in history have so many revolutionary advances been made in such a short period of time, and never has medical treatment had a brighter future. With each new advance a death-blow is being dealt at man's common enemy—Disease. Nowhere has this been more clearly shown than in the Far Eastern campaigns of the Second World War, where countless lives were saved which in another age would have been lost.

It is therefore gratifying at this time to follow the history and romance of medical science in the ensuing pages. From its early conception to its present state it is a story of singular interest. How disease has progressively been recognized, prevented, and treated is a fascinating tale, which has its human as well as its scientific aspects.

It is sometimes difficult to realize the intense opposition which greeted many of the most far-reaching discoveries, notably in the causation of infection. Medicine is a most conservative profession, and in older times a rigid obedience to the accepted teachings often tended to delay the advance of the science. As Sir Thomas Browne said, in his *Religio Medici*, "the mortallest enemy unto knowledge, and that which hath done the greatest execution upon truth, hath been a peremptory adhesion unto authority."

To-day, however, problems are considered in a more enlightened manner, and each suggestion is met with the knowledge that a new age is upon us, and boundless possibilities are ahead. With the innovation of the sulpha drugs, and the even greater wonder of penicillin, who knows but that in the not-too-distant future we may well have specific therapeutic agents for the cure of tuberculosis and cancer, to mention only two of the scourges that still remain unconquered? Intensive research

is being conducted along these lines, and the hopes of millions are with these workers in their noble crusade.

As the author has rightly indicated, the great difference between medicine and other sciences is that it has brought only relief of suffering to all mankind. No other science has been devoted so whole-heartedly and so unstintingly to the cause of humanity, and certainly no study has paid such rich humanitarian rewards. Medicine to-day has reached a new peak, and the united efforts of all mankind are at long last being directed against man's oldest and most inveterate enemy.

ALEXANDER FRANKLIN

INTRODUCTION

SCIENCE has lost much of its romance. With each new discovery and invention it has become a more dangerous weapon, a two-edged sword that can be used equally for good and for evil. (Science means knowledge, and the price of knowledge is responsibility. It rests with mankind to decide whether science will ultimately prove a blessing or a curse.

It is refreshing, therefore, to turn to one branch of science that has brought nothing but good. When Robert Louis Stevenson gave Dr Jekyll his profession it was a happy choice; for there is no Mr Hyde in the history of medicine. Its scientists have quarrelled furiously among themselves, but all have been bound by a single common purpose: to seek not merely knowledge, but knowledge that will help humanity.)

The history of medicine is the story of unselfishness and team-work. The scientists have not worked in secret, patenting their discoveries for financial gain. Indeed, nothing more effectively gives the lie to the suggestion that scientific progress depends on economic incentive. Far from seeking personal advantage, medical scientists have gone out of their way to persuade their colleagues to follow up their researches. From the earliest beginnings to the present day, medicine is the story of free exchange of knowledge and *esprit de corps*.

It must not be imagined, however, that the medical profession is one big happy family. Nothing could be further from the truth. Doctors are human, and the worst enemy of every science is the universal human failing of opposition to new ideas. In every age the larger part of medical progress has been achieved by a few original thinkers flying in the face of the accepted teachings of their day. They have had to suffer bitter criticism and hostility, and great strength of character has been needed for them to force their discoveries on an unreceptive community. Even in the nineteenth century four of the very greatest discoveries in the history of medicine—the germ

theory of disease, the antiseptic method, vaccination, and anæsthesia—were all violently opposed by the bulk of the medical profession. It is said that people are wiser to-day; that is a question only history will be able to decide. Meanwhile, it should not be forgotten that the Victorians had the same idea about themselves.

Yet this conservatism is not without its value. At least it ensures that no theory can be generally accepted until it has been submitted to very severe tests. Nowhere is caution so necessary as in medicine, and the brake on progress has also prevented the adoption of entirely false principles.

As will be seen in the pages that follow, there is a curious tendency on the part of people to attribute discoveries to chance or luck. There has been much careless writing about so-called scientific accidents, especially in medical research. This belittlement of great discoveries is thoughtless and unjust. No 'accident' has ever led to anything unless its significance has been grasped and its possibilities explored by the scientist. As Louis Pasteur said, "Chance only favours the mind that is prepared."

Finally, it must be said that although as much as possible of the romantic history of medicine has been crammed into this volume, ruthless selection has been unavoidable. The stories of dental and veterinary surgery, to mention only two, have had to be left out altogether. Many other subjects have had quite inadequate attention, and the author realizes that the book can serve only as an introduction to the story of the most colourful and fascinating of all the sciences.

PATRICK PRINGLE

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THE ORIGINS OF MEDICINE

MEDICINE was the first science because it was the most urgent. Death, fever, and pain—these were the mysteries that concerned prehistoric man before ever he began to worry about the stars and the waves. A sick man cried for help; the man who went to answer that cry was the first doctor.

Prehistoric man left few records. Some odd bones, a few crude drawings on rocks, a strange array of 'surgical instruments'—that was all. From such information, coupled with observation of the primitive peoples that survived civilization, many romantic stories have been woven. The accounts differ, and none is wholly reliable; but a few fairly dependable facts have been established.

Why, asked man, did he die? Why did he get pains and fevers? These were difficult questions to answer. He knew nothing about disease, and had little idea of how his body functioned. All sickness and injury was mysterious. A blow from another man, a bite from a savage animal, a stone from an enemy's sling—these were visible causes of pain and death, but still magical in origin. Primitive man made no essential difference between death or injury caused by a seen weapon or a falling tree and the sudden fever or abdominal pain. In both cases the primary cause was the same: magic.

Prehistoric man accepted the obvious solution. If some of his physical woes were caused by living beings, then so must the others be. The beings that caused disease were of a different kind. They were invisible, they struck suddenly and without warning, there was no easy defence against them. They were greater, wiser, more powerful than man himself. He called them spirits and demons.

Thus man explained the problem of death and disease in the same way as the problem of the world about him. Spirits were

everywhere. They made the sun shine, the seas move, the rivers flow, the winds blow—and they made his limbs ache and his body sweat and finally cease to function altogether.

The enemy struck with his sling because he was angry. Why did the demons strike? They, too, must be angry. One could strike back at the enemy, unless he was too powerful—then he had to be appeased. The demons were much too powerful.

So the first medical treatment took the form of placation of invisible spirits.

The Medicine Man

The good doctor, or Medicine Man, was the one who could get the best terms from the demons. He was the most skilled in magic, he knew all the best charms and talismans, he uttered just the sort of incantations that pleased the demons most. A really first-class doctor, of course, would appease the demons in advance, and thus keep his tribe in health and strength. Even then prevention was valued above cure.

There were no medical text-books, so doctors had to learn from experience. Some herbs, it was found, had magic of their own which could be used to counteract the magic of the demons—provided their application was accompanied by the correct magic ritual. A fractured leg could be much less troublesome if immobilized with a few sticks of wood. A demon lodged in the muscles could be wheedled out simply by rubbing and stroking—we call it massage.

Medicine was beginning.

The Birth of Surgery

Prehistoric man used to get headaches. Sometimes they went away of their own accord, but sometimes they got worse. Then it was time to consult a doctor. The Medicine Man had no difficulty in making a diagnosis. He recognized the headache as a symptom; the cause was just another demon which had somehow found its way into the patient's brain. The headache might have followed a crack on the skull, which was a common occurrence in those days, or it might have come on in the

middle of the night. That made no difference. There was no knowing with demons.

In some cases the patient responded to the usual treatment of charms and incantations. Others were more stubborn. The demon was unable to get out by the same mysterious means which had enabled him to get in, and he kept on tapping and banging until somebody did something about it. There was only one thing that could be done in a case like this. The Medicine Man called in a surgeon.

After a preliminary examination the surgeon prepared to operate. Selecting a sharp piece of flint, he cut through the skin and into the bone. He had no saw, so he had to carry on the operation with a single instrument. He scraped away at the bone until a hole was made right through it. He had to go carefully at the end. Some of his older colleagues had been careless enough to interfere with that grey matter underneath—and the demon didn't like that!

The operation was finished. The hole was made, and it was presumed that the demon made its way out. Then the wound was dressed with leaves and grass, and the patient began his convalescence. Sometimes he died, but not always. Skulls unearthed by archæologists have shown clear evidence of the bone having healed after this operation.

Headaches were by no means the only disorders that called for this treatment. Epiletic fits were also traced to a demon in the head, as were most cases of mental disease.

The operation is known as 'trepanning,' or 'trephining.' It is still practised by primitive tribes in some parts of the world, but almost exclusively for the treatment of head-injuries. Nor is the practice confined to primitive peoples; for modern surgeons perform this very operation in cases of what is called depressed fracture of the skull, to relieve pressure on the brain from a piece of splintered bone.

Early Civilization

The medical profession, like all other professions, was a product of civilization. So far as is known, there were four main

civilizations in ancient times, and little was recorded about the beginnings of any of them. In historical survey it is customary to begin with that of the part of Asia known as Mesopotamia. The inhabitants of this region invented an alphabet, and it may be assumed that there was some sort of medical literature. This, unfortunately, has not come down to us, and the only other records are those of the "Father of History"—the ever readable, but not always truthful, Herodotus.

One fact, however, is certain: there were still demons. Invocation of spirits remained the standard treatment, and the administration of herbs was considered as of secondary importance. But herbs could sometimes cure, whatever was said during their application, and successful prescriptions were written down on clay and passed on from one generation to the next.

The Babylonians practised dissection of animals, and showed an especial interest in the liver of the sheep. They can hardly be said to have founded comparative anatomy, however, as their interest in this organ was prompted rather by a desire to read into the future. All the same, surgery was taken fairly seriously, as may be seen from their variety of instruments, which included saws and chisels as well as different sorts of knives.

The most notable medical relic of the Babylonian civilization is contained in the famous laws of King Hammurabi, who reigned some twenty centuries before the birth of Christ. He laid down a fixed scale of doctors' fees, which varied, as now, according to the means of the patient. Thus, for the successful incision of an eye abscess a nobleman was to be charged ten shekels; while for the same operation a merchant had to pay only half the amount, and a slave was given the same treatment on the payment of two shekels by his master. The emphasis was on the word 'successful.' If the patient lost the sight of his eye as a result of the operation it was quite a different story, and the doctor had to pay for his mistake. The penalties varied in much the same way as the rewards. If the nobleman lost his sight, the doctor lost his hands; while any accident to the slave called for nothing worse than replacement by one of the doctor's own slaves.

As ten shekels was equivalent to roughly £2, it would seem likely that a good many noblemen had to put up with their eye abscesses!

Egyptian Doctors

Prehistoric man had his good spirits as well as demons—life would hardly have been worth living if he hadn't. The Egyptians went one better, and had a special God of Medicine. His name was Imhotep, which means 'he who cometh in peace.' He did not rise to the rank of deity until long after his death. In his lifetime he was physician to King Zoser, who lived some thousand odd years before Hammurabi of Babylon. In addition to his medical duties Imhotep held an office something like that of Prime Minister. He was also an architect, and one pyramid he built near Cairo can be seen to this day. His reputation was tremendous, and he was worshipped for centuries. He was, it is said, "the good physician of gods and men, a kind and merciful god, assuaging the sufferings of those in pain, healing the diseases of men, giving peaceful sleep to the restless and suffering." Unfortunately absolutely nothing is known about this medical career, so how far his fame was justified cannot be said.

A little more is known about another physician of the same period. This was Nenk-Sekmet, and the inscription on his tomb records that he "healed the king's nostrils." No case-notes, however, were appended.

Yet in comparison with the other ancient civilizations the records of Egyptian medicine are remarkably extensive. The majority of these were discovered only in the last century, the most famous being the 'Ebers papyrus,' which was found between the legs of a mummy in a tomb in Luxor, on the banks of the Nile. It was compiled about 1500 B.C., and is more in the nature of a medical encyclopædia than a simple text-book. It is full of the most elaborate prescriptions, and one at least of the favourite ingredients has not lost its popularity (and unpopularity)—castor-oil. The prescriptions, however, were regarded as quite useless unless accompanied by solemn incantations to spirits. The treatment of cataract, for example,

consisted of the application of verdigris ointment dissolved in "beetle honey," to the accompaniment of the following words:

> Come, verdigris ointment! Come, verdigris ointment! Come, thou verdant one! Come to him and take from him the water, the pus, the blood, the pain in the eye, the blindness, the flow of matter which are worked there by the god of inflammations

—and a good deal more in the same strain.

The Egyptians do not appear to have known much anatomy and physiology, and they seem to have missed a golden chance of furthering their knowledge of the body in their practice of embalming. Certain of the internal organs had to be removed from all prospective mummies, but dissection for the advancement of medicine was apparently forbidden. Even so, the Egyptians had a good knowledge of practical surgery, notably in the treatment of fractures and dislocations. Their bandaging, too, was extremely skilful.

Specialism in medicine is no new idea. The Egyptians were very keen on it, according to Herodotus. "The art of medicine," he wrote, "is thus divided amongst them: each physician applies himself to one disease only, and not more. All places abound in physicians; some physicians are for the eyes, others for the head, others for the teeth, others for the parts about the belly, and others for internal disorders." Even that did not satisfy everybody, for a certain monarch is recorded to have had two ophthalmologists at his service—one for each eye!

Egyptian doctors put much faith in diet in the treatment of disease, and especial importance was attached to hygiene. It was the influence of the Egyptians that later led the Jews to formulate the sanitary laws that abound in the Old Testament.

Medicine in India

According to some authorities the Hindu civilization is even older than the Egyptian. Their earliest existing medical records, however, were compiled many centuries after the Ebers papyrus. The most famous is called the 'Ayur Veda.' Like the Egyptian writings, this was the work of a number of different doctors.

The two best-known contributors were Charaka and Susruta, who lived some five hundred years apart.

India is very rich in medicinal herbs, and it was only natural that a large part of the book should be taken up with prescriptions. As with the Egyptians, these were invariably accompanied by invocations to spirits. But the most striking feature of the early Hindu doctors was their great surgical knowledge. Surgery, which was in such low repute in Europe in the Middle Ages, was regarded by Susruta as "the first and best of all medical sciences; less liable than any other to the fallacies of conjectural and inferential practice; pure in itself, perpetual in its applicability; the worthy produce of heaven, the certain source of fame."

It is significant that the early Hindus practised dissection of the human body, although the practice was subsequently forbidden. Anatomy was included in the Ayur Veda, and the section on surgery was very detailed. More than a hundred instruments were described, including forceps, lancets, catheters, and probes. As regards operations, the most common was lithotomy, or the removal of a stone from the bladder. Fractures were splinted with bamboo, and hæmorrhage was arrested by the direct application of heat to the blood-vessel. The latter method is known as 'cauterization,' from the Latin word meaning 'to burn.'

The surgeon was enjoined to wear his hair short, keep his nails clean, and wear a sweet-smelling dress. (Not till the nineteenth century was the wisdom of this advice understood.) In operating he was not to perspire, shake, or make exclamations. The best time for operations, it was said, was when the sky was clear and the new moon near at hand. Students, according to Charaka, should be taught "to be chaste and temperate, to speak the truth, to obey their teacher in all things, and to wear a beard." They learned the technique of surgery by practising on wax models, water-bottles, and cucumbers.

As regards the treatment of diseases, diet and hygiene played a large part, and physicians attached considerable

importance to taking the pulse. But perhaps the most notable feature of early Hindu medicine was the founding of 'Houses of Benevolence,' or hospitals. The centre of these was at Benares, where a medical school was also established. The credit for this work is generally ascribed to King Asoka, who set up hospitals for animals as well as for human beings.

Medicine in China

Nowhere was medicine so closely identified with magic as in China. This is apparent from the fact that demons are still believed in to this day. If the more advanced doctors have given up incantations, their patients haven't.

When drugs were in short supply the Chinese physicians had an ingenious method of 'treatment' which has been reported in very recent times. This consisted simply of inviting the patient to swallow a piece of paper on which the prescription was written out. As the incantation remained the same, good results were often claimed!

The medical profession must have been in very high esteem in ancient China, for the two earliest-known doctors were Emperors. These were Shen Nung, who lived about 3000 B.C., and Hwang Ti, who was born a few centuries later. Both these august physicians wrote books, and in China to-day these are still referred to quite extensively. Shen Nung wrote mainly on drugs, but Hwang Ti was more scientific and included some primitive anatomy and physiology. His theories were generally very far from the truth, because for the Chinese dissection was completely taboo. For the same reason surgery was never of a high standard. In one form of treatment, however, the Chinese excelled: that was massage, and it is recorded that they were the first people to use the blind for this work.

2

THE FATHER OF MEDICINE—AND HIS FAMILY

LIKE the Egyptians, the early Greeks had a God of Medicine. He, too, began life, as it were, as a mere mortal, about the year 1250 B.C. His name was Æsculapius. A Chief of Thessaly, he served in the Trojan Wars, and is believed to have invented an instrument for removing arrowheads from wounds. In civilian life he was not a court physician like Imhotep, but had a public clinic in the famous Temple of Delphi, where he performed miraculous cures. Indeed, he was so successful in his practice, ran the legend, that Pluto, God of the Underworld, made a formal complaint to the all-powerful Zeus; if Æsculapius went on at this rate, argued Pluto, mortals might stop dying altogether. Zeus saw his point, and sent down a thunderbolt which killed Æsculapius.

The story has a happy ending, however. After his death Æsculapius was deified, and even given a daughter, Hygeia, who was appropriately known as the Goddess of Health. Apparently Zeus raised no objections to his continuing his profession posthumously, and it was natural that he was even more successful as a god than he had been in his lifetime. A number of temples were raised in his honour, the most famous being at Epidaurus; and on the tablets there were inscribed the stories of the extraordinary cures wrought by the physician after his death. The method was for the sufferer to go to the temple and spend the night there, while the resident priests offered up prayers. Then Æsculapius would appear in the form of a dream and give the necessary treatment.

The case-histories make remarkable reading. One patient went to the temple with only one eye; Æsculapius applied a little ointment—and the man left in the morning with two good eyes. Even more noteworthy was the case of the "son of Hermione," who was blind in both eyes. A temple dog, acting

under divine instructions, licked his eyes, and his vision was fully restored. Finally, Æsculapius surpassed himself in his original treatment of a case of dropsy. It was a single brief surgical operation that has never been attempted since, and—it is hoped—never will be again. The god cut off the man's head, turned his body upside down, let the water run out, set him back on his feet, and replaced the head!

It need hardly be added that not a single case of failure was recorded at Epidaurus.

The legend of Æsculapius persisted for many centuries, and his symbol—a snake twined round a staff—forms the basis of the crest of most present-day medical bodies, notably the R.A.M.C. The drawing on the title-page of this book is a copy of the symbol.

The Dawn of Science

Magic was still the dominant factor in early Greek medicine, but even in the time of Æsculapius there were signs of a more scientific outlook. The war surgery described in Homer's *Iliad*, for example, is essentially practical. Homer, who lived about 1000 B.C., was not a medical man; but the brief accounts he gave of treatment of wounds showed that surgery at least was becoming more rational.

The Greeks' whole attitude to life was becoming more rational. They were the first people to make a serious study of the meaning of the universe, of Nature, of life and death—and of disease. The easy explanation of spirits and demons did not satisfy them.

One of the earliest rational physicians was none other than Pythagoras, better known for his contributions to mathematics. He made only a small contribution to medical knowledge, apart from a few prescriptions, chief of which were diet and gymnastics for the maintenance of health; but he founded a medical school, and taught his pupils to study the structure and functions of the healthy body in order to know how to treat the body in disease.

Pythagoras was born in 580 B.C., and in the next century the influence of his teaching made itself felt in every science in

ancient Greece. At least one of his school deserves mention as representing the new medical outlook. This was Empedocles of Agrigentum, who spent his time studying the human body instead of working out new prescriptions for drugs. Empedocles was not a modest man. "I am revered by both men and women," he asserted, "who follow me by ten thousands, inquiring the road to boundless wealth, seeking the gift of prophecy, and who would learn the marvellous skill to cure all kinds of diseases." After these extravagant claims it is not surprising to learn that Empedocles still had some belief in spirits and demons, and the value of his work suffers accordingly. Even so, he left some interesting descriptions of the organs of the body, of which he regarded the heart as the centre and the blood as the source of heat. His practical work was still more useful. By drainage of swamps and the lighting of huge bonfires he prevented the spread of a malaria epidemic in quite a 'modern' fashion.

The Father of Medicine

Empedocles may be regarded as representative of the very best in Greek medicine of his time. The change that took place less than half a century after his death may therefore be regarded as nothing short of a complete revolution. Demons and spirits were utterly banished, magic was discarded, charms and incantations disappeared from medical treatment; theories gave way to scientific reasoning, and medical practice was held to be valid only when based on definite facts and observations. In short, medicine became a science. The man who was the unchallenged leader of this revolution has appropriately been given the title of "Father of Medicine," and his name was Hippocrates.

Hippocrates was born in the year 460 B.C., on the little island of Cos. His father was a physician, and he himself was alleged to have been a direct descendant of Æsculapius—although that story need not be taken very seriously. Like Æsculapius, he held an open-air clinic, but there the resemblance ends. For no man did more to destroy the mischief of the Æsculapius legend than Hippocrates.

At the time of his birth there was already a medical school of sorts in Cos, which he attended as a student. Later he was to teach in the same school, but a good deal of his life was spent in travelling. He lectured and practised in Athens and other big Greek cities. Plato, who lived about the same time, praised him highly, and his fame was such that he came to be known as "Hippocrates the Great." Strangely enough, the date of his death is obscure. All authorities agree that he was at least eighty years old when he died, and some suggest that he was over a hundred.

Hippocrates had no biographer, and the details of his life are scanty. But what is far more important is that his great teachings were handed down in a permanent form. The *Corpus Hippocraticum*, or 'Hippocratic Collection,' consists of over a hundred works, all concerned solely with medicine. True, they were not all written by Hippocrates himself; a number of contradictions are to be found in the different books, and the standard varies a good deal. But many of the major treatises were undoubtedly his own, and the spirit of his teachings pervades the works that were later added by his disciples.

The Hippocratic Collection is no mere historical curiosity, like the Ebers papyrus and the writings of the early physicians of India and China. It is full of knowledge and wisdom, and is as fresh to-day as when it was written. The Hippocratic ideals and general principles require no lip-service; they are quoted to-day in the medical lectures of university professors all over the world. Indeed, no summary could possibly do the Collection justice, and quotations from the text are better than any commentary.

Signs and Symptoms

According to Hippocrates, the most important thing in the practice of medicine was observation. This sounds a very ordinary statement nowadays, but it must be remembered that in his time doctors were apt to regard the patient as of little importance. Hippocrates changed all this. "First," he instructed, "the physician must examine the face of the patient,

and see whether it is like the faces of healthy people, and especially whether it is like its usual self." Every little action of the sick man, he maintained, threw some fresh light on his disease. Hippocrates's own powers of observation were almost uncanny. He drew inferences not only from obvious physical signs such as fever, breathing, and change of complexion, but from the patient's expression, manner, voice, and even position in bed. His observation was equalled by his gift for description, and the signs that indicate the approach of death have come to be known as the 'Hippocratic facies'—

> Nose sharp, eyes hollow, temples shrunken, ears cold and with their lobes turned outward, the skin of the face parched and tense, the colour yellow or very dusky.

It is difficult to believe that the case-book of Hippocrates is nearly 2400 years old. Every important detail is recorded in an objective, scientific manner that has never been bettered. The following example is typical:

> In Thasos the wife of Delearces, who lay sick on the plain, was seized after a grief with an acute fever with shivering. From the beginning she would wrap herself up, and throughout, without speaking a word, she would fumble, pluck, scratch, pick hairs, weep and then laugh, but she did not sleep; though stimulated, the bowels passed nothing. She drank a little when the attendants suggested it. Urine thin and scanty; fever slight to the touch; coldness of the extremities.
>
> *Ninth day.* Much wandering, followed by return of reason; silent.
>
> *Fourteenth day.* Respiration rare and large with long intervals, becoming afterwards short.
>
> *Seventeenth day.* Bowels under a stimulus passed disordered matters, then her very drink passed unchanged; nothing coagulated. The patient noticed nothing; the skin tense and dry.
>
> *Twentieth day.* Much rambling followed by recovery of reason; speechless; respiration short.
>
> *Twenty-first day.* Death.
>
> The respiration of this patient throughout was rare and large: took no notice of anything; she constantly wrapped herself up; either much rambling or silence throughout.

The "rare and large" breathing is now called the Cheyne-Stokes respiration, after the two physicians who investigated it in the nineteenth century. An even better description of the same thing, showing imagination as well as powers of observation, is given in another of Hippocrates's case-sheets, in which he notes that "the respiration throughout was like that of a person recollecting himself."

Next in importance to observation came what is known as prognosis. This is simply an attempt to see into the future by scientific methods. Hippocrates wrote a book on prognosis, which he based on observation, experience of past cases, and reasoning. "I hold that it is an excellent thing for a physician to practise forecasting," he said. "He will carry out the treatment best if he knows beforehand from the present symptoms what will take place later." In another passage he summed up the duties of the physician as follows: "Declare the past, diagnose the present, foretell the future; practise these arts. As to decisions, make a habit of two things—to do good, or at least to do no harm."

Methods of Treatment

Hippocrates's attitude to treatment was summed up in one of his most famous sentences: "Our natures are the physicians of our diseases." He recognized that medical skill at its height would never be more than a supplement to the healing-power of Nature—a fact that was 'rediscovered' only in recent times. He was strongly opposed to the indiscriminate use of drugs, and his own prescriptions were comparatively few in number. He attached immense importance to diet, which, he said, should be full in winter but more sparing in summer. Sedentary people were advised to eat less than more active workers, and Hippocrates revealed a fine appreciation of the relation between food and energy. "The performances of work are directed to the consumption of what exists, while food and drink are intended to replenish void." Rest was a great factor, and hot baths were frequently prescribed. He was fond of giving purgatives, and his other common forms of treatment

included gargles, hot fomentations, and poultices. For fevers he prescribed barley-water. Even in the light of modern medicine most of his general principles still hold good.

"What cannot be cured by medicine must be cured by the knife," and Hippocrates's contributions to surgery were of the highest standard. Most important was the introduction of the principle of extension in the treatment of fractures. When a bone is fractured it often happens that the broken ends overlap, and unless this is quickly remedied a gross deformity will result. By the use of various forms of apparatus, including beams, chains, and a number of different wooden structures, Hippocrates pulled the two ends apart, set them in their correct position, and then splinted the fracture. His splinting has been awarded high praise, while his treatment of dislocations was not very different from the methods employed to-day.

Hippocrates laid down very exact instructions for the preparation of an operating-theatre:

> Operative requisites in the surgery: the patient; the operator; assistants; instruments; the light, where and how placed; the patient's person and apparatus. The operator, whether seated or standing, should be placed conveniently to the part being operated upon and to the light. Each of the two kinds of light, ordinary or artificial, may be used in two ways, direct or oblique.

In the treatment of wounds Hippocrates remained faithful to his belief in the healing-power of Nature, and applied mainly soothing salves. He was a skilled surgeon, and performed lithotomies as well as other internal operations. He maintained that no head-injury could be regarded as trivial, and for depressed fractures of the skull he performed the trephine operation. Like Susruta of India, he attached great importance to the surgeon's care of his finger-nails. We now know that countless lives were lost through the non-observance of this teaching until its truth was scientifically demonstrated by Lord Lister less than a hundred years ago.

Medical Science

Hippocrates was not only a clinician. He was the Father of Medical Science as well as of Medical Practice. Completely rejecting the time-honoured demon-theory, he made the first attempt to find a rational explanation for the cause of disease. His predecessor Empedocles had propounded the theory of four 'elements'—fire, earth, air, and water; applying the same idea to medicine, Hippocrates suggested that the body had four 'qualities,' which he named as dry, moist, hot, and cold, and four 'humours,' *viz.*, blood, phlegm, black bile, yellow bile. Derangement of one or more of the humours caused sickness, and thus the problem of diseases was explained.

The reasoning was false; but the fact that the theory was based on reason instead of superstition made it a great advance on the demon-theory. It must be remembered that germs had not been discovered, nor could they be until a microscope was invented. Hippocrates came nearer the truth in his study of the sources of disease, which he attributed to the air, water, and climate, and he drew up practical rules of hygiene and sanitation on this basis.

Hippocrates also studied anatomy and physiology. Whether or not he practised dissection cannot be definitely stated, but it is certain that he had few facilities for doing so. It must be admitted that his contributions to anatomy and physiology were not very great. He rightly regarded the brain as the centre of consciousness, and observed that the blood flowed through the heart. He had no idea of the nervous system, however, and never suggested that the blood might circulate. He did not distinguish between veins and arteries, while nerves, sinews, and ligaments were all grouped together under the general heading of 'flesh.'

The Hippocratic Oath

By no means the least important of Hippocrates's contributions to medicine was his famous oath, which still forms the basis of the ethics of the profession to-day. Hippocrates brought to medical practice a dignity hitherto unknown. "Medicine,"

he asserted, "is of all the arts the most noble"—for to him it was an art as well as a science. But a high standard could only be maintained if physicians proved worthy of their calling, and his instructions to his followers were very exacting. "Life is short, the art long; opportunity fleeting, experiment dangerous, and judgment difficult. The physician must be ready, not only to do his duty himself, but also to secure the co-operation of the patient, of the attendants, and of the externals." To-day, when medical students walk in the quadrangle at Edinburgh University, an engraving on the wall reminds them of the first part of this truth.

The physician was further enjoined to dress neatly but simply, to shun perfumes, to be courteous and calm and, above all, honest. His private life had to be above reproach, and he was to make sure his fees were proportionate to the patients' means. He must be humble, for "the physician is the servant of the art."

On entering the profession he had to take an oath. This oath is too long to quote in full, but the following extract will suffice to show how little the ethics of the profession have changed in the last twenty-four centuries:

> I swear by Apollo the Physician, by Æsculapius, by Hygeia, by Panacea, and by all the gods and goddesses, making them my witnesses, that I will carry out according to my ability and judgment, this oath and this indenture. . . . I will use treatment to help the sick according to my ability and judgment, but never with a view to injury and wrong-doing. Neither will I administer a poison to anybody when asked to do so, nor will I suggest such a course. Similarly I will not give to a woman a pessary to cause abortion. But I will keep pure and holy both my life and my art. . . . Into whatsoever houses I enter, I will enter to help the sick, and I will abstain from all intentional wrong-doing and harm, especially from abusing the bodies of man or woman, bond or free. And whatsoever I shall see or hear in the course of my profession, as well as outside my profession in my intercourse with men, if it be what should not be published abroad, I will never divulge, holding such things to be holy secrets. Now if I carry out this oath, and break it not, may I gain for ever reputation among

all men, for my life and for my art; but if I transgress it and forswear myself, may the opposite befall me.

The Influence of Hippocrates

The most important result of the work of Hippocrates was the establishment of medicine as a science. It must be remembered that at the beginning of his career the most popular clinics were still the Temples of Æsculapius. Belief in magic died hard, and it needed considerable courage for a physician to stand up and say there were no such things as demons. Hippocrates knew this, and he even devoted a whole treatise to the study of the very disease that lent itself most to the demon-theory—epilepsy. Because of what seemed its obvious demoniac origin, it was popularly called "the sacred disease"; and the opening words of Hippocrates's book are characteristic:

> I am about to discuss the disease called sacred.
>
> It is not, in my opinion, any more divine or more sacred than other diseases, but has a natural cause, and its supposed divine origin is due to man's inexperience, and to their wonder at its peculiar character. . . . If it is to be considered divine just because it is wonderful, there will not be one sacred disease but many, for I will show that other diseases are no less wonderful and portentous, and yet nobody considers them sacred.

Hippocrates believed in the divine, but not in demons. "Things are not in varying degrees divine or human, but God is in all things." As for epilepsy, "the nature and cause of this illness arises precisely from the same divine origin from which all else proceeds."

Hippocrates hated nothing more than guesswork. He tried to find a reason for everything, and when none was apparent he frankly confessed his ignorance. His modesty was striking. He never boasted, and was not in the least ashamed to record his failures as well as his successes. Indeed, out of forty-two cases described no fewer than twenty-five ended in death. At the end of one of these he added, "I have written this down deliberately, for it is valuable to learn of unsuccessful experiments, and to know the causes of their non-success."

Perhaps Hippocrates's greatest merit was his love of humanity. And perhaps the greatest of his many great sayings was:

"Where there is a love of man there is also a love of the art."

Later Greek Medicine

All great men are misunderstood, and Hippocrates was no exception. His most fervent admirers were as guilty as his opponents; for after his death Hippocrates was paid the doubtful honour of being made a god. One can imagine what his feelings would have been had he been told in his lifetime that he was destined to be placed on the same lofty pinnacle as his supposed ancestor, Æsculapius!

The Hippocratic spirit remained, although the standard of medical practice declined. At that time the Greeks were engaged in wordy battles over all the sciences, and 'schools of thought' and sects were springing up everywhere. Medicine came in for its share of the wrangling, and was treated more as a philosophical study than as a practical profession. Observation was largely neglected, and the leaders of each sect were more concerned with their own pet theories than with treating any patients. The most faithful disciples of Hippocrates did little to improve this state of affairs. Hippocrates was a god, so his Collection became a Bible, and any divergence from it was heresy. This school of thought neglected the simple general principles, and pored over the Master's few theories, giving them a variety of strange interpretations. Their intentions were good, but it would have been more in the Hippocratic teaching if these followers had abandoned this slavish fidelity and started to think for themselves.

In the fourth century B.C., however, a new impetus was given to medicine by Plato's most famous pupil—Aristotle. The son of a court physician, he was not a practising doctor himself, but included medical science in his comprehensive studies. Natural history led him to the dissection of animals and fishes, from which he deduced important facts about the human body. He made a number of mistakes. While he recognized the heart as the origin of the blood-vessels, he thought it was also the

centre of the nervous system. The brain he regarded as nothing more than a 'sponge' to cool the heart. He also adopted and elaborated the theories of the four elements, qualities, and humours.

Aristotle's main importance, however, lay in his insistence on the scientific method. "Health and disease," he affirmed, "also claim the attention of the scientist, and not only of the physician, in so far as an account of their causes is concerned."

Back to Egypt

After Aristotle the glory of Greece began to fade. One of Alexander the Great's last achievements was the foundation of the city that bears his name, and it was in Egypt that civilization was continued. The civilization remained Greek, however; and in the first real medical school in the world the teachings were those of Hippocrates.

Mainly as a result of the influence of Aristotle, the two basic branches of medical science were founded in Alexandria. These were anatomy, or the study of the structure of the human body—the 'geography' of the body, as it were; and physiology, the study of its functions. Both these new sciences were made possible only by the introduction of the practice of dissection of the human body, which had been forbidden in the time of Hippocrates.

The "Father of Anatomy" was a Greek named Hierophilus, who was born at the beginning of the third century B.C. He is reputed to have dissected no fewer than six hundred dead bodies, and his discoveries had a tremendous influence on subsequent medical research. He confirmed Aristotle's theory that the heart was the centre of the blood-supply, but declared that the nervous system originated in the brain. He distinguished between arteries and veins, and made the important point that the former as well as the latter contained blood. (Arteries had previously been regarded as containing only air, because they were found to be empty in a dead body.) Hierophilus also made a special study of the pulse, which he regarded as of great importance in examination of a patient, and he counted it with

the aid of a water-clock. Once he was asked to define a good physician, and his reply was brief and to the point:

"He who knows how to distinguish between the possible and the impossible."

The "Father of Physiology" was another Greek, Erasistratus, who lived at the same time as Hierophilus. His views differed from those of his colleague in many respects. He adhered to the old theory that the arteries contained only air, and he considered that the liver played an equal part with the heart in the supply of blood. In other respects, however, Erasistratus was well in advance of Hierophilus. By far his greatest achievement was his observation of two distinct types of nerves—sensory and motor. This was a discovery of the first magnitude, although it was not realized as such until many centuries later. Erasistratus also described the valves of the heart, and he was the first medical scientist to dispute the theory of the four humours, which Hierophilus had accepted. He ascribed the cause of disease to an excess of blood—yet, oddly enough, he strongly opposed the general custom of bleeding patients whenever they were ill. In treatment he closely followed the Hippocratic teachings, insisting on a sparing use of drugs, and he attached much importance to hygiene for the prevention of disease.

The school of Alexandria flourished for many years, and a vast collection of medical books was acquired. Not one of these has survived. The whole library was burned by a mob of barbarians, and the 700,000 manuscripts, it is said, kept the town supplied with hot water for a period of six months.

3

MEDICINE UNDER THE ROMANS

BY the first century B.C. the centre of civilization had shifted again—this time to Rome. But medicine still remained Greek, not only in spirit but in actual practice; for nearly all the great physicians of the Roman era were natives of Greece.

Medicine under the Romans was at first a very sorry affair. Long after the death of Hippocrates there were still no genuine doctors in Rome, as all practice of medicine was forbidden by law and religion. But people fell ill, and a sick man instinctively seeks help; so there were bound to be doctors of a sort, and the only effect of the law was to drive the profession underground, as it were. In these circumstances no respectable citizen would think of taking up such a disreputable vocation, and thus the early Roman doctors were, without exception, quacks and charlatans. Spirits and demons were found everywhere, and almost the only treatment of disease consisted of the liberal use of incantations and drugs. There was an amazing variety of the latter, popular prescriptions including such ingredients as crocodiles' dung and the blood of bed-bugs!

Greek doctors made their first appearance in Rome about the beginning of the second century B.C. As may be imagined, it was no love of their neighbours that drew them there, but merely a desire to 'get rich quick' at the expense of the ignorant but wealthy Romans. From both practical and ethical viewpoints, therefore, their standard was low. The more intelligent Romans realized this, and strongly urged their countrymen to have nothing to do with these foreigners. Cato the Censor, a wise old statesman, who hated all physicians and all Greeks, treated himself and his family on highly original lines. He prescribed cabbage for practically every ailment except dislocations, which he found to respond better to "magical songs."

"Prince of Physicians"

It was not until the year 90 B.C. that the first reputable Greek doctor arrived in Rome. His name was Asclepiades, and he built up such a successful practice that he came to be known as the "Prince of Physicians." Born in Bythnia, he was educated at Athens and attended the medical school at Alexandria. He was thirty-four when he reached Rome, and he was quickly marked out as very different from the usual type of Greek doctor. It is said that his reputation dated from the occasion when he astounded the Romans by apparently restoring a dead man to life. This occurred during a funeral procession which Asclepiades happened to meet. His keen eyes detected a sign of life in the 'corpse,' and he stopped the procession and gave the man some treatment. After this his fame spread rapidly, and before long he was counting among his friends such men as Cicero and Mark Antony.

By his own account Asclepiades had no time for the teachings of Hippocrates. He scorned the idea of trusting to Nature to cure diseases, describing the principle as "merely a meditation on death." Yet his own methods were Hippocratic in spirit. His treatment showed a marked preference for diet, massage, and rest to the administration of drugs. He was a keen and patient observer, and was responsible for the classification of diseases as acute and chronic.

The physician's aim, said Asclepiades, should be to cure disease *cito, tuto, et jucunde*—quickly, safely, and agreeably. He rejected the theory of the four humours, but probably only because it was his habit to contradict practically everything Hippocrates had said. He made no contributions to anatomy or physiology—dissection of the human body was strictly forbidden by the Romans. Like Hippocrates, again, he regarded the climate as a major factor in the cause of disease, and even asserted that "the inhabitants of Britain were long-lived because the climate prevented the dissipation of the innate heat of their bodies"!

For all his opposition to Hippocrates, Asclepiades did a good

deal more for medicine than the Master's docile followers. It was ironical that he, who was so contemptuous of orthodox schools of thought, should have been made the model of a new sect that was formed after his death.

A New Text-book

The first medical text-book written in Latin appeared about A.D. 30. The author was a Roman, and therefore not a doctor. His name was Aurelius Cornelius Celsus, and he was a gentleman of leisure who spent most of his life in the study of philosophy and science. His medical work was entitled simply *De Re Medicina*, and is largely an orderly summary of all the teachings of the Greeks. Celsus professed to be a follower of Asclepiades, but in the main he tried to reconcile the teachings of the latter with those of Hippocrates and Aristotle.

Even though he was not a practising physician, Celsus added a number of observations on his own account. From the two volumes on surgery it seems probable that he secretly practised dissection. He made useful contributions to the knowledge of anatomy, notably on the structure of bones. He described a variety of operations, including the 'modern' excision of the thyroid gland in cases of goitre, and also one for the removal of tonsils. Eye operations and dentistry were also included. Like Erasistratus of Alexandria, Celsus was strongly opposed to the practice of blood-letting, which was coming more and more into vogue. "It is not a new thing to let blood from the veins," he wrote scathingly, "but it is new that there is scarcely any malady in which blood is not drawn."

Celsus deplored the way in which the study of medicine had been split into opposing sects, and his work was an attempt to restore unity to the profession. He failed, probably because he was neither a doctor nor a Greek; and it was left to the greatest figure since Hippocrates to accomplish this necessary work.

Galen, 'the Peaceable'

Claudius Galenus, to give him his full name, was born in A.D. 131, in the town of Pergamus, in Asia Minor. His name

may be translated as 'the peaceable,' and no description could be more unsuitable. Aggressive, dogmatic, passionate, quarrelsome, quick-tempered—these were some of the attributes of the last of the great doctors in the Greek and Roman civilizations. That Galen was great is beyond doubt; he ranked second only to Hippocrates, and it is to his eternal credit that for all his boasting he never pretended to be higher.

Galen's father had first intended him to study philosophy, but as a result of a dream he changed his mind and decided to make young Claudius a doctor. The boy was seventeen when he began his studies. Pergamus was then the second largest medical centre in the world, but he was not satisfied until he had studied at the largest, which was still Alexandria. He also visited Greece, thus obtaining the best medical education possible in those days.

Galen began to write at an early age. When he was twenty-one he had six medical treatises to his name, and during his lifetime he increased this number to five hundred, of which over a hundred have survived. As a young man he was confident and probably conceited, but from the first he expressed his complete faith in the principles laid down by Hippocrates. In many respects he was the kind of follower the Father of Medicine would have liked. He realized the great worth of the teachings of Hippocrates, and grasped the important fundamentals; but he was too sensible to regard six-hundred-year-old theories as sacred, and followed the spirit rather than the letter of the Hippocratic Collection.

In A.D. 162 Galen arrived in Rome. Marcus Aurelius was Emperor, and the civilization was at its height. The arts and sciences were followed with as much zeal, if not the same ability, as they had been by the Greeks. Medicine, however, still lacked form. The sects and schools of thought were more numerous than ever, and their differences had widened with the passage of time. Fierce arguments were going on, and little scientific progress was being made. Without hesitation Galen flung himself into the fray, supporting no one and attacking every sect in turn, in a bold, insolent manner that aroused

hostility from all sides. He was scornful of the theories of Hierophilus and Erasistratus, spoke contemptuously of "the absurdities of Asclepiades," and found fault with the teachings of every one except Hippocrates.

He was a brilliant doctor. He needed to be, if he was to stop in Rome. His practice was far greater than that of Asclepiades, and he was soon the most famous physician in the first city in the world. For some unexplained reason, however, he returned to Pergamus after a few years. But Marcus Aurelius, wisest of the Emperors, saw that Rome needed him, "We have but one physician, Galen," he said. Galen returned to Rome, to the joy of his patients and the discomfiture of his numerous opponents.

Scientific Research

Galen's main achievement was to fill in the gaps of the Hippocratic Collection on the subjects of anatomy and physiology. In this work he made frequent use of the discoveries of the Alexandrian School, which he sometimes praised, as well as attacked. He sought to find the cause of every bodily function, and his method was experimental. He had studied the human skeleton in Alexandria, but in Rome dissection of the human body was still forbidden. He therefore pursued his researches on the bodies of animals. His passion for dissection knew no bounds. His subjects were usually apes, as they resembled the human species most; but in his quest for knowledge he dissected numerous other animals—including, it is said, an elephant!

Galen confirmed Erasistratus's distinction between sensory and motor nerves, and explained the relation between nerves and muscles. He traced the main cause of paralysis to injuries of the spinal cord, he gave a correct description of the phenomenon of the human voice, and he explained much of the mechanism of the eye. All this met with much opposition and open disbelief on the part of his opponents—and Galen, the fiercest of critics, did not take kindly to criticism of himself. "When I tell them all voluntary movement is produced by muscles controlled by nerves coming from the brain," he complained, "they call me a teller of marvellous tales."

Galen discovered that the kidneys secrete urine. He confirmed Hierophilus's repudiation of the theory of Aristotle about the brain cooling the heart, and investigated both these organs. He also followed Erasistratus's theory of the relation of the liver to the supply of blood, and made a careful and detailed study of the whole question of the blood-system. (This will be described later, in the chapter on the discovery of the circulation of the blood.)

Galen was always a scientist. He regarded treatment of symptoms as superficial, and stated that a successful cure must be related to the cause. He professed complete faith in the healing-power of Nature, although in practice he used drugs far more extensively than Hippocrates had advised. He emphasized the importance of diet, massage, and baths, and understood something of the value of the rays of the sun. In addition to normal observation he invariably took the patient's pulse, and gained useful information from this method even though he had no idea of the meaning of the little throbs he felt in the wrist. His surgery was sound for his time, although he did not introduce any important new operations.

Errors and their Effects

Galen made mistakes. He repeated the Hippocratic doctrine of the four humours, and many centuries were to pass before anyone had the courage and initiative to suggest that two such great authorities could be wrong. In both anatomy and physiology he neglected the fundamental differences between the bodies of animals and those of men. His theory of the flow of the blood, as will be seen later, was quite inadequate. Possibly his worst error, however, was in the treatment of wounds. He regarded suppuration as a natural part of the healing-process, and coined the unfortunate phrase 'laudable pus.' Surgery was clouded by this erroneous theory right up to the time of Lister.

Galen died in the year A.D. 200, and his influence remained the dominant factor in medicine for the next twelve centuries. His achievements were tremendous. He broke up the futile sects and schools of thought, and re-established medicine as a

science. He codified all Greek and Roman medicine from the time of Hippocrates, weeded out many of the false theories, and made considerable contributions of his own.

Yet Galen's influence was not wholly for the good. His great fault was that he made no provision for further progress. He was not so modest as Hippocrates. He knew all the answers. He was so confident and dogmatic, and at the same time so obviously brilliant, that he left little opportunity for criticism. He thought he had said the last word on medicine, and he was so convincing that every one else thought so too. His teaching was followed far more strictly than that of Hippocrates had been, and so long as this attitude prevailed, progress was impossible. A typical example of the way Galen brought medical science to a standstill was given by a Byzantine physician named Paulus of Ægina. This highly competent doctor wrote a book in seven volumes, based largely on the teachings of Galen. It was a good practical manual, so far as it went, but it lost much of its value when the author concluded with the complacent statement that his work contained nothing original because all that could be said about medicine and surgery had already been said.

It needed another Galen to break down that attitude.

Pro Bono Publico

It has been shown that medicine under the Romans was Greek in origin, spirit and actual practice. The Romans themselves, however, were responsible for work of a somewhat different nature that was of the greatest importance to medical practice. This included the establishment of the first state medical service the world has ever known, the introduction of the first organized hospital system, and the foundation of civic hygiene and sanitation.

The Roman state medical service sounds quite up to date nowadays, except that it functioned without the financial backing of a national health insurance scheme. 'Panel' doctors were appointed by the Government and assigned to all the large towns and rural centres, each doctor being responsible for the care of a certain number of inhabitants. His services were

given free to the poor, and he was paid out of the Treasury. In fact, his status was similar to that of a civil servant of the higher grade.

The first Roman hospital is believed to have been founded as far back as the third century B.C., on the Island of St Bartholomew—from which, of course, 'Bart's' in London got its name. By the time Galen came to Rome the hospital system was already extensive; while for the wealthier classes there were private nursing-homes. Roman hospitals were very different from the Indian 'Houses of Benevolence' or the Egyptian and even Greek temples. The wards were separated by long corridors, a refectory or dining-hall was situated in the middle of the block, while at one end were separate annexes for administration, dispensary, stores, and staff quarters.

There were military as well as civilian hospitals, and the armies in the field were equipped with the equivalents of Regimental Aid Posts and Advanced Dressing Stations. The one drawback to the Roman Army Medical Service was that the surgeons were given the rank of N.C.O. only.

Roman hygiene and sanitation were of a very high standard. Great importance was attached to water-supply, and many of the wonderful aqueducts constructed are still standing—and still used—to this day. Plumbing was remarkably good, private houses had their own water-cisterns and taps, and waste pipes led into a network of sewers. There were public baths, with hot and cold water, and public and private lavatories with water-flushes. Finally, drainage of marshland was carried on extensively.

LIGHT IN THE DARK AGES

AFTER the Greek Empire broke up, its culture was continued first at Alexandria and then at Rome. When the Roman Empire broke up, culture disappeared from Europe for a thousand years.

Galen was the last of the great physicians. After the death of Marcus Aurelius the Roman civilization began to crumble, until it was no longer able to withstand the attacks of the Huns and other barbarians. Rome itself became untenable. The seat of government was transferred to Constantinople—and with it went the science of medicine.

The medical schools disappeared. The Greek manuscripts were lost or destroyed. Medicine was no longer a science—it was not even a profession. For centuries it seemed as if Hippocrates and Galen had laboured in vain.

As a natural result demons and spirits returned in full force. Diagnosis, prognosis, and rational treatment were replaced by charms, incantations, and a variety of weird and wonderful 'drugs' that compared unfavourably even with those of the earliest Romans. A cure for cancer, for example, was honey mixed with the gall of a goat. Rheumatism was treated with spittle and songs, gout with cow-dung, epilepsy with mistletoe-berries. One prescription for an eye complaint ran, "Take a live crab, put his eyes out, and put him alive again into the water, and put the eyes on the neck of the man who hath need; he will soon be healed."

Magic was supplemented by inferences drawn from the moon and the stars, and as long as a thousand years after the death of Hippocrates the Archbishop of Canterbury issued a solemn warning that "it is very dangerous to let blood on the fourth day of the moon, because both the light of the moon and the tides are upon the increase." That such theories were not

confined to laymen is well illustrated in the description of the "doctor of phisike" in Chaucer's *Canterbury Tales*:

> With us there was a doctor of phisike;
> In all this world, ne was there none him like
> To speake of phisike and surgerie,
> For he was grounded in astronomie.

In the Middle Ages hygiene scarcely existed. There were no drains, few baths, fewer lavatories, and an abundance of dirt. There was no proper water-supply, no plumbing, no sewage. Such sanitation as existed in Europe would have appalled any self-respecting Roman of Cæsar's time. Disease, in consequence, was rife. Epidemics raged everywhere, the worst being the notorious "Black Death," or plague, in the fourteenth century, which claimed the lives of one out of every four inhabitants of the civilized world.

The Influence of Christianity

The only place where learning was kept alive was the monastery. Knowledge was copied rather than studied, and there was no genuine progress; but at least some part of the Greek and Roman literature was preserved for later generations.

But the monastery's contribution to medicine was not confined to the labours of the scribes who copied out manuscripts, few of which were of a medical nature at all. What was far more important was that it offered sanctuary and hospitality to the poor and the needy—and the sick. Thus the monastery also became a hospital; and it is to the medieval Christian Church that we owe many of our present-day hospitals, notably St Bartholomew's and St Thomas's.

Monks might not have been medically skilled, but as nurses they performed their duties with unstinting devotion. While medical science was non-existent, medical practice was enriched with an entirely new quality—the Christian ideal. Charity, in the highest sense of the word, was the key-note of the monastery hospital, and lack of medical knowledge was partly offset by the spirit of self-sacrifice and true brotherly love. A historian's account of

the work of the Church in an epidemic of plague is typical of this:

> Many of our brethren, by reason of their great love and brotherly charity, sparing not themselves, cleaved one to another, visited the sick without weariness or heed-taking, and attended upon them diligently, cured them in Christ, which cost them their lives, and being full of other men's maladies, took the infection of their neighbours.

The brethren may never have heard of Hippocrates, but their services were invaluable if only because "where is a love of man there is also a love of the art."

Women as well as men devoted their lives to the cause of humanity, and one of the most famous of the Christian healers was the Abbess of a large convent in Germany. She is known to us as St Hildegard, and after her death legends arose about her 'miraculous' cures. She herself made no such claims in the book she wrote, which consisted mainly of prescriptions. Many of these were no better than other medieval recipes, but she made one big advance in the administration of drugs: she made them taste better. Her pills were not sugar-coated, but she took away the unpleasant taste of her concoctions by mixing them with flour and serving them up as pancakes. Hildegard was a good deal more than a nurse, and may be regarded as one of the earliest lady doctors.

The Eastern World

Europe was in darkness, yet the light of knowledge had not been completely extinguished. Many of the works of Hippocrates, Galen, and other Greek physicians had been safely evacuated to Constantinople, where they were carefully perused and transcribed. Most diligent of the copyists were the Nestorians, a Christian sect which was finally expelled from the town. They took their manuscripts with them—no longer in the original Greek, but translated into their own language, Syriac. They fled to Mesopotamia, the home of the ancient Babylonian civilization, and founded a medical school and a hospital at Jundi-shapur.

This was in A.D. 431, and for more than three hundred years their precious treasures attracted little outside interest. But in that time was born Mahomet, the Prophet of the Arab world, and a new civilization sprang up after him. All over the Near and Middle East there was a desire for knowledge and learning, and the science of medicine began again. Thanks to the Nestorians, it did not have to start from the beginning. The manuscripts were translated into Arabic, and the spirit of Greece lived again.

The centre of Arab culture was the city of Baghdad, whose enlightened Caliph founded a university, a hospital, and a medical school. In later years no fewer than eight hundred and sixty doctors were practising in Baghdad, while the civic hospital services were staffed by eighty physicians. One of the earliest of these was Hunain Ibn Ishaq, who made translations of the works of Hippocrates and Galen, for which he was offered their weight in gold. Hunain added some works of his own, notably on the study of the eye and its diseases. On one occasion he was ordered by the Caliph to prepare a poison; he was not bound by the Hippocratic Oath, but he accepted its principles and refused the command. The Caliph was so impressed that he immediately appointed him court physician.

The Arabs did not add a great deal to medical science. They realized the tremendous value of the literature they had so fortunately acquired, and at first they were content merely to study and follow these teachings. Later they grew bolder and added commentaries; and some, like Hunain, wrote original works of their own. Their opportunities for research were limited by the strictest ban on dissection, and their surgery suffered accordingly. Their most important scientific advance was in the realm of chemistry, which was born of the pseudo-science of alchemy.

Progress was further hindered by the reverence for Galen that characterized all their writings. The Arabs were not very critical, and Galen's mistakes received the same acceptance as his genuine discoveries. It would be unfair, however, to blame the Arabs for this. Their culture started late, and it was to

their credit that they had the sense to benefit from an earlier civilization. They were bound to accept the superior knowledge of the Greeks, and it was a good thing that they chose Galen as a master rather than a leader of one of the numerous narrow sects that abounded in Greece and Rome.

Two Great Physicians

Two at least of the Arab physicians were outstanding, and their influence was later to play a large part in the revival of learning in Europe. The first of these was known as Rhazes, so called after the Persian town of Rai, in which he was born in A.D. 860. He wrote a twenty-five-volume medical encyclopædia, based largely on the works of Galen, and over two hundred other books. His most important treatise was entitled "On the Small Pox and Measles," which made the first recorded distinction between these two diseases. He was a more original thinker than most of the Arab doctors, and he made several improvements in the practice of medicine and surgery, notably with the introduction of animal gut in sutures, or stitches, for abdominal wounds.

Although he did not begin to study medicine until he was forty years old, Rhazes quickly made a name for himself, and was invited to choose the site for the new hospital which the Caliph planned to build in Baghdad. Rhazes's method was original but by no means irrational. He took a number of pieces of meat and hung them in different parts of the town; the one that remained fresh the longest marked the site for the hospital.

Another case reveals that Rhazes was also something of a psychologist. The patient was a prince, and his complaint was rheumatism, which he said was so bad that he could not walk. Rhazes tried various forms of treatment without success, and formed the opinion that the trouble was not entirely physical. In the course of one of his visits to the prince's dwelling he was informed that the invalid was taking a bath. Thereupon Rhazes rushed into the bathroom, brandishing a sharp knife, and threatened to kill the prince. So convincing did he appear that

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THE TITLE-PAGE OF THE BOOK OF VESALIUS

his patient ran out of the room, leaving his clothes and his rheumatism behind.

The second great Persian physician lived a century later, and his name was Ibn Sina, which was contracted to Avicenna. Unlike Rhazes, he began his medical studies at a very early age, and was appointed court physician when only eighteen. He had an adventurous career, and he was accorded the same title as Asclepiades of Bythnia had enjoyed—"Prince of Physicians." His fame rests mainly on his *Canon of Medicine*, which was used as a text-book in European medical schools long after the Renaissance. He resembled Galen in many ways, even to the point of daring to quarrel with some of his teachings, and had much the same confident and convincing style.

Avicenna attended at the courts of a number of Persian rulers, and he so impressed one prince by his successful cure of colic that he was given the post of Prime Minister as a reward 'for services rendered.' It was not a popular appointment, and the Army protested. The prince needed the Army, and Avicenna was no longer necessary now that he had cured the colic; so the physician was removed from his post as suddenly as he had been given it. The story had a sequel, when the prince got another attack of colic, and Avicenna was given a second brief term of office.

Avicenna made a number of valuable contributions to medical science, although he also added some very unscientific theories. One of these was based on his acceptance of a popular belief in the healing-power of colours. As the blood was moved by red bodies, he said, all treatment for disorders of the blood should be of a red colour.

Return to Europe

The Moslem Empire was not confined to the East. It extended to southern Spain, and it was from Cordova that knowledge began to flow back into Europe. At first it was a trickle rather than a stream. Cordova had a university in the eighth century, and in the year 1000 it boasted several hospitals and medical schools, with a large number of practising physicians.

One of the latter did much to remedy the low standard of surgery that was one of the major defects in Arab medicine. This was Albucasis the Moor, and he wrote a practical and well-illustrated text-book on the subject. His outlook was very realistic. He divided surgical operations into two classes—"those which benefit the patient, and those which usually kill him."

Jews as well as Arabs practised in Cordova, and it was they who first spread enlightenment in Europe. They had their own translations of the writings of the Greeks, which were turned into Latin and distributed to other towns in Europe. Not until the eleventh century, however, was any real interest shown in the works of the ancients, and then it was in Italy that the new era in medicine began.

The School of Salerno

The medical school of Salerno came into being in the eleventh century. Christian monks were the first teachers, but it was another Moor who brought the knowledge of the Greeks to the town. Constantine, as he was called, was a bit of a fraud, for he passed off most of his translations as his own original works. The fact remains that it was he who first brought the classics back to Italy, and thus rendered medicine an invaluable service.

Salerno flourished in the twelfth century, and its fame became so great that it was recognized as the only medical centre in the whole continent. At the beginning of the next century the word 'doctor' was first used for physicians, and in 1240 the Emperor Frederic II enacted a law that established medicine as a profession once again.

"Considering the harm which may arise from the ignorance of physicians," ran the law, "we ordain that no one shall henceforth practise physic unless he be first publicly examined by the masters at Salerno." A preliminary three-year course in logic was introduced, and the study of medicine itself was extended to five years. The curriculum was based mainly on the translations of Hippocrates and Galen, while a special

section was devoted to surgery, which Frederic regarded as a branch of medicine. (This view was in advance of his times; until the eighteenth century surgery was generally regarded only as a trade, and was practised mainly by barbers.) Finally, the Emperor ordained that the poor should be treated free, and doctors applying for licences were required to take an oath very reminiscent of that of Hippocrates.

The main work done at Salerno consisted of reviving knowledge rather than adding to it. This was a very necessary preliminary work, and it is not surprising that no great advances were made. Equally inevitable was the over-faithfulness to the recognized masters, notably Galen. The doctrine of the four humours was accepted without question, and all the old mistakes were repeated over and over again. But much useful work was done in Salerno, especially in the establishment of a medical library and the training of doctors.

The best known of the writings of the teachers at the school is the poem *Regimen Sanitatis*, said to have been the joint work of four physicians. It presented medical knowledge in a simple and attractive form, and had a pleasant flavour of wit and philosophy. As the title implied, it was concerned more with the maintenance of health than the cure of disease. Two couplets may be quoted as typical:

> Joy, Temperance, and Repose
> Slam the door on the doctor's nose.
>
> A King that cannot rule him in his diet
> Will hardly rule his Realm in peace and quiet.

Another interesting book written at Salerno was *The Doctor's Visit*, a very business-like manual on how a physician should go about his job if he wanted to make a good living. Its ideals could scarcely be called lofty, but much of the advice was very shrewd. When taking the pulse the physician was told to bear in mind that "it may be affected by your arrival, or, the patient being a miser, by his thinking of the fee. . . . Do not be in a hurry to give an opinion," it went on, "for the friends will be more grateful for your judgment if they have to wait for it.

Tell the patient you will cure him, with God's help, but inform his friends that the case is a most serious one." The last sentence was rather subtle, and an explanation was added. "If the patient recovers, your reputation is increased; if he succumbs, people will not fail to remember that you foresaw the fatal termination of the disease."

Montpellier and Bologna

The school of Salerno began to lose its influence in the thirteenth century, but already other important medical centres had sprung up, at Montpellier and Bologna, where the good work was carried on.

The medical school at Montpellier probably began in the twelfth century, although the university was not officially recognized until 1289. One of its earliest teachers was Arnald of Villanova, who had studied and taught at Salerno and helped to compose the *Regimen Sanitatis*. He wrote a text-book of treatment far in advance of anything produced by the Salerno school. His teaching generally was very sound. "The moderate and wise physician," he wrote, "will never hasten to drugs unless compelled by necessity." More open to argument was the opening sentence of his book on poisons, which read:

"In this book I propose, with God's help, to consider diseases of women, since women are poisonous creatures."

By now the study of medicine was no longer confined to the Latin countries, and Englishmen were going to Italy and France to study at the new schools. One of the best known of the Montpellier graduates was John of Gaddesdon, who afterwards taught at Oxford and was physician to the English court. He was one of the first Englishmen to write a medical text-book, which he called *Rosa Anglica*, or *The English Rose*. Unfortunately it was not a very good book. The author was not averse to using the demon theory to explain anything he did not understand, the prescriptions given were liberally interspersed with incantations and ritual.

The University of Bologna was founded before that of Montpellier, but the medical faculty was not introduced until the

thirteenth century. It was there that dissection was at last reintroduced, although in its early form it was of no scientific value. Medicine was still based on the 'sacred' writings of Hippocrates, Galen, and even Avicenna, and it did not seem to occur to physicians that they might be able to find out anything more. No serious researches were made, and dissection was used only to demonstrate the old ideas of anatomy and physiology. The very way it was done made it impossible to be otherwise. The lecturer regarded it as beneath his dignity to cut up a dead body, and was content to deliver his lecture while a junior performed the dissection and another assistant pointed to the appropriate organs with a stick. The students were not invited to take an active part in the proceedings.

This method of dissection continued until the fourteenth century, when one of the professors startled his colleagues by performing dissections himself. This was Mondino di Luzzio, and his treatise on anatomy did much to restore that branch of medicine to its rightful place. His anatomy was by no means accurate, as it was inevitably based on the work of Galen; but his book was important in that it drew the attention of doctors back to this basic science.

Medieval Surgeons

Not all the teachers at Bologna followed Galen so docilely. Two, at least, had the courage to voice doubts about the generally accepted theory of 'laudable pus.' The first of these was a bishop as well as a doctor, named Theodoric. He wrote a book on surgery, which contained a passage that might well have been written in the nineteenth century:

> For it is not necessary, as Roger and Roland have written, as many of their disciples teach, and as all modern surgeons profess, that pus should be generated in wounds. No error can be greater than this. Such a practice is indeed to hinder nature, to prolong the disease, and to prevent conglutination of the wound.

Theodoric was followed at Bologna by a Norman, Henri de Mondeville. He appreciated the classics, but was not afraid to

criticize them. "God did not exhaust all his creative power in making Galen," he observed, to the horror of the more orthodox of his colleagues. Mondeville taught at Montpellier as well as Bologna, and he made a creditable attempt to restore surgery to its proper place in the profession. His opposition to the 'laudable pus' theory deserves to be quoted, like that of Theodoric, if only because of its significance in more recent times:

> Many more surgeons know how to cause suppuration than how to heal a wound.
>
> Wash the wound scrupulously free from all foreign matters; use no probes, no treatments—except under special circumstances; apply no oily or irritant matters; avoid the formation of pus, which is not a stage of healing but a complication. Wounds dry much better before suppuration than after it.

It would be an exaggeration to credit Bologna with the origin of the antiseptic idea, but a later chapter in this book will show just how remarkable Mondeville's teaching really was.

A more famous surgeon than either Theodoric or Mondeville was Guy de Chauliac, a pupil of the anatomist Mondino di Luzzio. He had been well taught. To quote an early translation of his works, "The same manner that the blinde man worketh in the hewynge of a log, so doth a cyrurgen that knoweth not the nathomye."

Chauliac's best-known book was entitled *Great Surgery*. It contained a number of advances over his contemporaries, especially in the use of extension for treatment of fractures, and a fair amount about dentistry, including instructions regarding the provision of artificial teeth. It also included some outspoken criticism of the classics. Chauliac accused the physicians of his day of despising "everything not sanctioned by custom or authority, forgetting that, as Aristotle declares, these are the two great hindrances to the discovery of the truth."

Chauliac performed one great disservice to medicine. Ignoring the teachings of Theodoric and Henri de Mondeville, he upheld the theory of 'laudable pus,' and treated wounds accordingly.

Before the Renaissance

The Dark Ages were over. The spirit of scientific inquiry had already been shown by Roger Bacon—who is said to have invented spectacles—and the German philosopher Albertus Magnus. Medicine was re-established in Europe. Other cities followed the example of Montpellier and Bologna, and new schools were set up in Padua and Paris. The essential preliminary of stock-taking was completed, and slowly and painfully original thought was at last returning. Standard works were still closely followed, but the uncritical veneration for the classics was already being assailed. Criticism was given a fresh impetus in 1483, the year of the sack of Constantinople, where the original writings of Hippocrates and Galen, covered with the dust of the centuries, were unearthed and brought back to Europe. They were compared with the existing editions, which were found to have been grossly mutilated in the course of the years. This was a natural result of the alterations that had been made in translation. The Nestorians had translated from the Greek into Syriac, which had in turn been translated into Arabic; the Jews had turned this into Hebrew, from which many of the Latin editions were prepared.

The classics were no longer sacred, because they were not the true classics after all. The teachers felt they had been fooled. They violently abused the Arabs whom they had formerly praised, and resolved not to trust even the original Greek writings until they had verified the facts for themselves. Such scepticism would probably have angered Galen; but Hippocrates, surely, would have welcomed the change.

5

THE RENAISSANCE

THE transition from the Middle Ages to what is called the 'modern' period of history began in the fifteenth century, when the printing-press was invented. Starting in Italy, and spreading rapidly over the Continent, came a new spirit, a new desire for knowledge and progress, which affected every art and science. Culture, luxury of the ancient Greeks and Romans, reappeared. It was a revival of learning, a rebirth—a Renaissance. Unquestioning acceptance of authority gave way to criticism and experimental inquiry; and medical science, which had scarcely progressed since the days of Galen, was quickly enriched by great new discoveries.

The Human Body

Before the Renaissance man was strangely ignorant about the nature of his own body. The main reason for this was that he had never had a chance to see it—except from the outside. Bones, muscles, joints, blood-vessels—these were forbidden territory once they had ceased to function. Until the restoration of dissection in Bologna, to seek knowledge from a dead body was illegal.

The greatest character in the Renaissance was Leonardo da Vinci. Primarily an artist and sculptor, he had a hand in almost every art and science. It was only natural that he should contribute to medicine as well as almost everything else, and he made a thoroughly scientific inquiry into the structure of the human body. Da Vinci left only note-books on this part of his work, but from these it is clear that he had begun the most urgent and difficult task that lay before the whole of medical science: the exposure and correction of Galen's errors.

It was a native of Brussels, however, who made the first comprehensive study of anatomy. This was Andreas Vesalius.

Born in 1514, five years before the death of da Vinci, he began studying anatomy while still a child, dissecting dogs and other animals out of sheer curiosity. His father was fairly well-to-do, and the boy had a good education by the standards of his day. Then he went to Paris, and studied anatomy under Jacobus Sylvius, a confirmed Galenist. Dissection had not yet appeared in the medical syllabus in France, and the young student had to brave the law if he wanted to see for himself what his teacher was talking about. His desire for knowledge was too keen to let the law stand in his way, however, and his search for specimens got him in some awkward situations. Cemeteries were his favourite hunting-ground; unfortunately the dogs of Paris had found them out before, and Vesalius had more than one fierce scrap with them over the matter of a few bones. On another occasion he had the audacity to steal a whole corpse from a public gibbet.

The Renaissance was young, and Italy was still the scientific centre of Europe. So to Padua went Vesalius, first to study but soon to teach; and at the age of twenty-four he was appointed a professor at the university. The enlightened Italians encouraged dissection, and by this method Vesalius taught the students and himself at the same time. After five years of intensive labour he published one of the most famous books in medical literature—*De Humani Corporis Fabrica.* "The greatest book ever printed, from which modern medicine dates," was the verdict of Sir William Osler, the eminent medical teacher and historian. Seven hundred pages long, and with truly copious illustrations, this masterpiece was to serve as the basis of medical teaching for centuries to follow. The structure of the various bones, the relation between the brain and the spinal cord, the functions of the heart and lungs and muscles and nerves—all these were described with tremendous details. Every statement and drawing was based on first-hand observation, and comparison with a modern work reveals amazingly few major discrepancies.

That Vesalius came in for some criticism was only to be expected. This young man had dared to cast doubts on the

'infallible' teachings of the great Galen—it was medical blasphemy! An idea of the profession's slavish acceptance of Galen's theories even at that time may be gained from a single sentence in Vesalius's book: "Not long ago, I would not have dared to diverge a hair's breadth from Galen's opinion." But what he had seen with his own eyes compelled him to diverge considerably. This was no reflection on Galen, whose anatomy was perforce based on the body of the ape. But that Galen could be wrong was unbelievable. That was the opinion of Vesalius's former teacher, anyway—for none was more bitter in attacking the young professor than Jacobus Sylvius of Paris.

The *Fabrica* was published when Vesalius was twenty-eight. The remainder of his life is shrouded in mystery. He suddenly resigned from his Chair at Padua and went to Madrid as court physician to the Emperor Charles V. In doing so he was deliberately forsaking the study of anatomy, for dissection was strictly forbidden in Spain in the days of the Inquisition. The living body could be tortured in the rack—but woe betide the man who dared to defile it once it was incapable of registering pain!

It is hard to believe that the one-time body-snatcher of Paris should submit to such restrictions indefinitely, yet there is no real evidence to prove the contrary. There is a legend that Vesalius's final dissection was of a patient who died on his hands, and that only after beginning the autopsy did he discover that the man's heart was still beating! This gruesome story sounds highly improbable, in view of Vesalius's undoubted medical knowledge. And as any dissection in Spain would have had to be done in the closest secrecy, it is even more unlikely that the anatomist should have been found out and sent on a pilgrimage to Jerusalem as penance—for so the legend goes. The Jerusalem pilgrimage was a fact, however; and on the return journey, in 1564, Vesalius died.

'Barber-Surgeons'

The barber's pole is a familiar sight even to-day. The spiral pattern of red and white lines, and the brass knob at the end, are known to every one. The meaning is less obvious, and the

inquiring mind may well ask just what this sign has to do with the business of haircutting.

The truth is that there is no connexion at all. The origin of the barber's pole goes back to the Middle Ages, when barbers, odd as it may seem, were also surgeons. The pole itself is a symbol of the bandage that was wound round the patient's arm prior to blood-letting; the brass knob represents the basin used to catch the blood.

The association between barbers and surgeons was not so ridiculous as it sounds. To-day there seems little comparison between the skill required for cutting a man's hair and that for removing his appendix; but to-day surgery is a highly skilled and highly esteemed profession. It has not been so for very long. While a physician was always a professional man, surgery was for centuries regarded as a mere trade. Like haircutting, it called for a certain amount of manual skill, and thus it was that barbers practised it to supplement their normal work.

In the fourteenth century a Guild of Barber-Surgeons was officially constituted, and the formal association of these two occupations was to last in England for nearly four hundred years. Not unnaturally, some barbers began to specialize, either in haircutting or surgery, although the majority were content to combine the two jobs. This 'specialism' led to the formation, in the same century, of a Guild of Surgeons. It must not be imagined that this was the result of a break-away on the part of the surgically minded barbers, however; it was more in the nature of a rival concern. It is true that the Guild of Surgeons agitated to get the barbers to stick to haircutting, but for this they were sharply rebuked by the Court of Aldermen of the City of London. The Barber-Surgeons prospered; the Surgeons were never much more than their poor relations.

The best surgery of the day was military surgery, and the first Englishman of any note in this branch of medicine studied on the battlefields of France. John of Arderne, as he was called, was a good practical surgeon, and on his return to England he worked up an unusually profitable practice. He did not subscribe to Galen's theory of laudable pus, and for his time he

was a comparatively clean surgeon, even going to the extent of cutting his finger-nails. He worked out a high moral code for surgeons, who were not all they might be in this respect, and urged them to attend the poor as well as the rich. It must be added, however, that he did not go so far as to suggest that the same treatment should be given for both. For cases of constipation among the rich, for example, he advised a fairly expensive prescription—"but if he is a pauper, he may just drink his own urine."

Surgery was the last existing branch of medicine to be affected by the Renaissance. The early part of the fifteenth century was unremarkable except for the promotion of the Guild of Barber-Surgeons to a Worshipful Company. Soon after this the Guild of Surgeons gave up the struggle, and the bodies were incorporated in one company in 1540. It must not be thought that this was a victory for the barbers. The man mainly responsible for the union, Thomas Vicary, was a very surgical barber, holding the appointment of sergeant-surgeon to the King. At his instigation the new constitution of the company clearly defined haircutting and surgery as two distinct trades, and members were compelled to practise one or the other. Vicary was the first Master of the united company, and he laid the foundations for later surgical practice.

Shortly afterwards the teachings of Vesalius reached England, and surgery began to be mildly scientific. The reorganized company instituted some sort of training in anatomy for its surgical apprentices; lectures and demonstrations were given, and dissections were included in the curriculum. In the succeeding years the all-important post of Master of the company was filled by men of education and ability. Most of these, like John of Arderne, had gained their experience as war surgeons. They published their case-books and observations, and these served as text-books for the apprentices for many years. The most notable of these works appeared in the latter half of the seventeenth century under the title of *Severall Chirurgicall Treatises*. The author was Richard Wiseman, who had served as surgeon to the Forces at sea as well as on land, and later became sergeant-surgeon to King Charles II.

The reputation of surgery had improved little, however. Surgeons were still tradesmen, however seriously they might take themselves. Their chief detractors were the physicians, who ought to have known better. At first they had treated barber-surgeons with mild contempt, but now they were beginning to resent their increasing medical pretensions. The physicians persuaded the King to forbid surgeons from giving "inward physic," and tried to establish a supervision over their activities. The company rose against this, and a change of king restored their former rights. It was many years, however, before the two branches of medicine were placed on the equal footing on which they stand to-day.

The days of the Company of Barber-Surgeons were numbered. Their fortunes fell, and they were especially hard hit by the new hospitals that were being built. The surgical members became restless. They knew they could not hope to be taken seriously by the physicians as long as they were connected, even nominally, with hairdressers. The barbers hastened the inevitable end by forming an ill-advised alliance with the Worshipful Company of Periwig-makers. This was too much for the surgeons, who broke away completely and were formed into a company of their own in 1745.

Ambroise Paré

Barber-Surgeons were not confined to England. The same system prevailed on the continent, and it was a barber-surgeon of France who put surgery into the picture of the Renaissance. The son of a cabinet-maker, Ambroise Paré was born shortly after the beginning of the sixteenth century. He had little education; he gained some knowledge as an apprentice, and a lot more in the hard school of experience. "Surgery," said Paré, "is learned by the eye and by the hands." While still a young man he was fortunate enough to get a job at the Paris hospital of Hôtel-Dieu. He spent three years there, and then volunteered for military surgery.

It was during the battle for Turin, in 1537, that Paré made a name for himself. Most of the casualties were caused by gunshot

wounds, for which a very drastic treatment was in vogue. Gunpowder was generally accepted to be poisonous, and the poison had to be burnt out. The standard method of treating such a wound, therefore, was by cauterization with boiling oil and treacle. Paré was new at the job, so he obediently followed the advice of his senior colleagues. One day, however, when casualties were exceptionally heavy, his stock of these valuable medical supplies ran out. Very distressed, he decided that he must give the poor fellows treatment of some sort, so he dressed their wounds with a hastily improvised compound of egg-yolk, oil of roses, and turpentine. He had little hope that such a poor substitute for boiling oil would be of much use, and fully expected the patients to be dead the next morning.

But the next morning Paré was amazed to find that the men were not only alive, but looking a good deal better than the earlier casualties who had been treated in the orthodox manner. The latter had developed the usual symptoms of pain and fever, and the expected inflammation had set in; those he had felt so sorry for, on the other hand, had no fever and comparatively little pain, and the wounds of many were already beginning to heal.

Now Paré's discovery was sheer luck. He had never questioned the boiling-oil method, nor was his peculiar prescription anything but a hurried mixture of the materials at his disposal. He had no claim to fame on that account. But it was not luck that made him translate his chance discovery into terms of practice. Gunpowder was not poisonous, whatever his learned colleagues might say. He did not hesitate to tell them so. "Abandon this miserable way of burning and roasting," he urged—and made himself thoroughly unpopular in consequence.

Paré lived before the age of science, and it was only natural that he should accept results at their face-value. Burning oil did not heal wounds; egg-yolk, oil of roses, and turpentine did. Never mind why. Perhaps an even better prescription might be found, thought Paré, and he conducted many experiments to this end. Later he reported good results from a mixture of white of egg, flour, chimney soot, and fresh butter!

Cauterization should be avoided wherever possible—of that

Paré was sure. It was widely used in his time, not only in the treatment of gunshot wounds, but also to stop bleeding after amputation. Paré abandoned this method in favour of a practice that had fallen into disuse—tying the arteries with pieces of cord or thread called ligatures (from the Latin word meaning 'to bind'). Other of Paré's innovations included the use of trusses for hernia, the invention of artery forceps, and the making and fitting of artificial limbs.

Meanwhile he was becoming famous. The physicians might look down their noses at this barber-surgeon, but the King of France was no snob when it came to his own physical well-being. Paré was summoned to the court, and there he stayed. In 1559, while attending the dying Henry II, he met Andreas Vesalius, who had been loaned for the occasion by the King of Spain.

Ambroise Paré was not a scholar, nor did he ever pretend to be. He refused to learn Latin and Greek, and was openly contemptuous of the university professors who read learnedly from books and had forgotten what it was like to treat a case themselves. Above all, he was simple and humble. "I dressed him and God healed him," he used to say when complimented on a successful case.

The Mission of Paracelsus

If I stoop
Into a dark tremendous sea of cloud,
It is but for a time; I press God's lamp
Close to my breast; its splendour, soon or late,
Will pierce the gloom: I shall emerge one day.

These were the words that Robert Browning put into the mouth of one of the most mysterious figures in the history of medicine—Philippus Aureolus Theophrastus Bombastus von Hohenheim, better known as Paracelsus. How far this man enriched medical knowledge is a matter of controversy, but at least he gave a new word to our language—'bombast,' from his fourth Christian name.

Bombastic he certainly was, but about his other qualities there is little agreement. Few physicians of the Renaissance

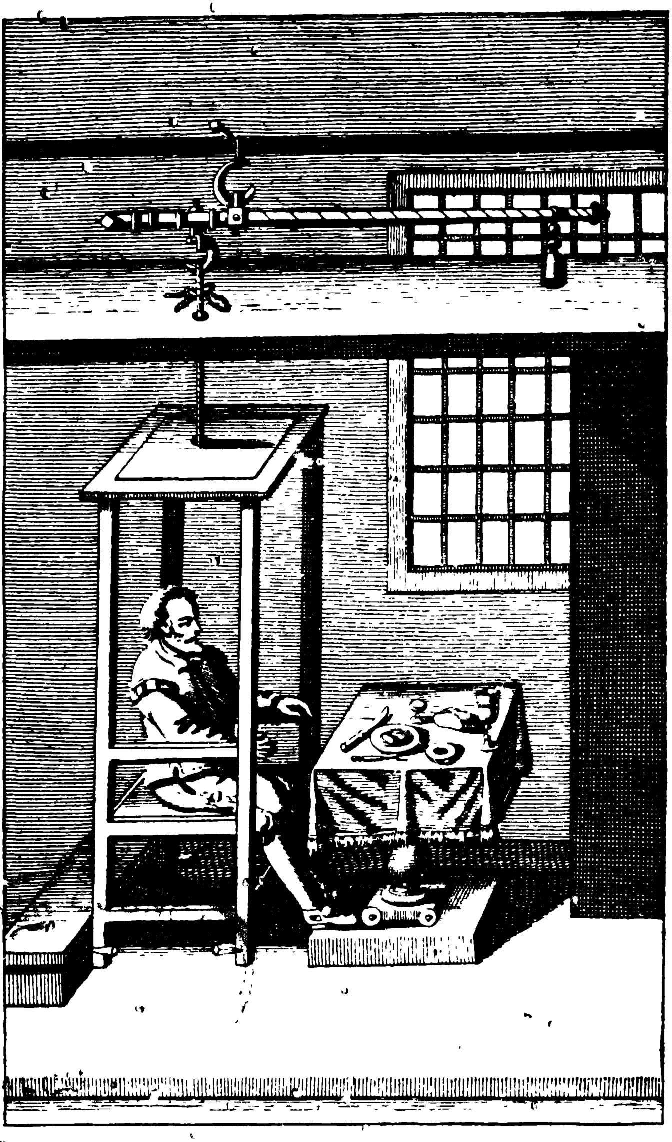
have received so much praise, and certainly none has been more severely criticized. Many reliable medical historians have dismissed Paracelsus in a few lines, as an unscrupulous charlatan who did nothing but harm. Other authorities, equally reliable, have paid him such compliments as "one of the founders of the modern period of medicine" and "the most original thinker of the sixteenth century"—and there was no lack of original thinkers in that age. Whether he was a great man or just a fraud, however, he was certainly very colourful.

He was born at Einsiedeln, in Switzerland, in 1493. His father was a doctor and his mother a hospital matron. He submitted to a rather haphazard education, attending irregularly at the University of Basle. Then, armed with a sharp sword and a sharper tongue, he started wandering over Europe, and a wanderer he remained for the rest of his life. "Reading never made a doctor, but practice is what forms a physician; for all reading is a footstool to practice, and a mere feather broom," he asserted in his usual graphic style. He is said to have taken a medical degree at Ferrara at the age of twenty-two, but this has never been definitely established. Indeed, the whole story of his life is enveloped in mystery, and accounts differ almost as widely as opinions on his merit.

Paracelsus travelled in countries as far apart as Sweden and Portugal, Egypt and Russia. He was at one time a war surgeon, and saw service in Holland and Denmark. His movements are difficult to trace exactly, because he avoided anything approaching a seat of culture or learning. Universities he hated, and he spent most of his time in the company of peasants, gipsies, and tramps—whom he considered far wiser than any professors. The professors, in their turn, had little time for him, and while still a young man he made a number of influential enemies.

He must have had some supporters as well, however, because when he returned to Basle at the age of thirty-three he was given the double appointment of lecturer at the university and city physician. In the latter post he exercised a supervision over the activities of the apothecaries, who were quickly enlisted into the ranks of his sworn foes. He angered the doctors by his blunt

AN ANATOMICAL FIGURE BY VESALIUS



SANCTORIUS SANCTORIUS IN HIS WEIGHING-CHAIR

From *Medicina Statica*, by Sanctorius Sanctorius (Padua, 1614)

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contempt, and got on the wrong side of the university authorities by lecturing in his native tongue instead of Latin. He did not remain at Basle for long. "I pleased no one except the sick whom I healed," he remarked later. He left the town for ever, and never again accepted a salaried appointment. He carried on wandering until he died at the age of forty-eight—and even the manner of his death was obscure. It was, like his life, a violent one; but whether it was the result of a drunken brawl, or whether he was deliberately murdered by his enemies, has never been established.

Paracelsus's fame rests on his defiance of tradition and authority. He was an avowed heretic, and he considered it his mission in life to destroy. His first lecture at Basle was dramatic. He entered the amphitheatre armed with the lecturer's usual array of books by Galen, Avicenna, and the rest. But he did not open them. "The buckles of my shoes," he told the astonished students, "are more learned than Galen or Avicenna." With much ceremony he set light to a bowl of sulphur and threw the books into the flames. "Thus will ye burn in hell," he added, rather unkindly.

Paracelsus attacked every recognized medical authority except one. This was Hippocrates, whom he rated second only to Paracelsus—which was very high praise indeed! With justification he maintained that Galen and Avicenna had distorted the teachings of Hippocrates, and he advocated a return to what he considered to be the true doctrines of the Father of Medicine. "The best of our popular physicians," he wrote, "are the ones who do the least harm. But unfortunately some poison their patients with mercury, and others purge or bleed them to death. A physician should be the servant of Nature, not her enemy." Knowledge of Nature, he maintained, was the foundation of the science and practice of medicine. Again, "Medicine is not merely a science, but an art; it does not consist in compounding pills and plasters and drugs of all kinds, but it deals with the processes of life, which must be understood before they can be guided."

All very true, but Paracelsus's own conception of the

"processes of life" was anything but scientific. Discarding the theory of the four humours, he propounded a queer, mystical theory of the relation between philosophy, astrology, and chemistry. In the last-named science, however, he made definite and important advances. He discovered hydrogen gas. He studied metals by working in the mines as an ordinary labourer, and discovered zinc. He introduced certain minerals, notably antimony, to medical treatment, and is said to have been the first to prepare laudanum.

As regards medicine, however, Paracelsus stands or falls by his sheer destructive criticism. He was a fanatic, an avowed rebel, and his self-appointed mission was to tear down what he considered to be false idols. Galen was his main target—and that Galen's influence had been holding back progress is now generally admitted. He was dogmatic and boastful, he invited criticism and enjoyed his notoriety. He did not expect to be understood in his lifetime; almost certainly he did not want to be.

Paracelsus has been dubbed the "other Luther." Perhaps the "other Galen" would be nearer the mark.

The Problem of Infection

The cause of infection is so well known to-day that it is difficult to realize how recently it was discovered. Coughs and sneezes spread diseases, as every child knows. He even knows why; infectious diseases are conveyed from one person to another by germs which live in the air and on his clothes. But germs are invisible to the naked eye, and the microscope was not invented till the seventeenth century. Until that came, disease had to remain a mystery, and so far only two possible explanations had been offered. One was the theory of demons and spirits; the other, Hippocrates's idea of four humours which were liable to be disturbed from time to time. Galen accepted the latter theory, and thus it became law for over a thousand years.

Before germs were discovered, however, the very fact that diseases came in epidemics had made people wonder. The

ancient Egyptians and especially the Hebrews probably knew a good deal more about it than their literature reveals. Many of the laws of hygiene in the Book of Leviticus could only have been directed against the spread of infection, and one passage in the Bible even suggests that the connexion between plague and rat-fleas was at least guessed.

The people of the Middle Ages were less enlightened. When epidemics appeared their only thought was flight from the affected districts. The result of this, of course, was merely a further spread of the disease. Hygiene and sanitation, as has been seen, were so primitive that a connexion between dirt and disease could never have been suspected. Disinfection was practically unknown, and such fumigation as was carried out was designed merely to destroy unpleasant odours.

It was recognized, however, that persons suffering from plague and leprosy were not good company, and isolation was introduced in the cruel form of banishment of lepers from human society. More practical and humane was the policy of the citizens of the Italian port of Ragusa, where incoming ships were not allowed to dock until they had stood by in the harbour for forty days, in Italian *quaranti giorni*—hence the word 'quarantine.'

It was not until 1546 that the first scientific theory of infection appeared, in a book entitled *De Contagione*, by Girolamo Fracastoro of Verona. It was a remarkable book for the period. Without any germ theory of disease to aid him, Fracastoro had to rely entirely upon observation and deduction. Yet his theory was remarkably 'modern.' He divided means of infection into three types—direct contact, contact with clothing and other articles, and infection at a distance. With no microscope at his disposal, he attributed the cause of infection to "invisible seeds," and went on to say:

> That these seeds are the carriers of the contagion and that they are the first origin of the disease there can be no doubt.
>
> It may be considered that the force of the disease lies in those seeds since they have the power to propagate and reproduce their own kind.

Nearly three centuries were to pass before Fracastoro's "seeds"—no longer invisible—were indeed proved to be the "carriers of contagion" by Louis Pasteur.

Fracastoro added the first scientific description of typhus fever, and he made the brilliant discovery that tuberculosis was an infectious disease. He had no means of proving his theory of infection, and it was not generally adopted in his time. The fact that he was working mainly in the dark only adds to the greatness of his achievement.

English Physicians

So many of the major discoveries in medicine have been made by Englishmen that one is apt to forget how late in history the science was brought to this country. Medical schools did not appear until long after Salerno, Montpellier, and Bologna. Even during the Renaissance any Englishman wishing to take up the profession was bound to study on the Continent. It was one of these physicians, Thomas Linacre, who persuaded King Henry VIII to found the first real medical association in the country—the Royal College of Physicians.

Linacre studied at Padua, in the late fifteenth century, and was one of the first students to have the opportunity of reading Aristotle and Galen in the original Greek. On returning to England he lectured on medicine at Oxford, and was appointed court physician. In 1518 he obtained the Charter of the Royal College of Physicians, which at last placed medical practice on a sound basis. Part of it ran as follows:

> Before this period, a great multitude of ignorant persons, of whom the greater part had no insight into physic, nor in any other kind of learning; some could not even read the letter on the book, so far forth that common artificers, as smiths, weavers, and women, boldly and accustomably took upon them great cures, to the high displeasure of God, great infamy of the faculty, and the grievous hurt, damage and destruction of many of the King's liege people.

One of Linacre's successors to the post of President of the college was John Caius, who also studied at Padua, where he

shared lodgings with Andreas Vesalius. He too became a court physician, and he lectured at the University of Cambridge. Influenced by Vesalius, he brought the study of anatomy to England. He also wrote a book on the "sweating sickness" which was endemic at that time. He still adhered to the theory of the humours which he had been taught, but rightly ascribed the spread of disease to lack of hygiene and sanitation.

A rather different character was Andrew Boorde, a graduate of Montpellier, who wrote a few interesting books mainly of the how-to-keep-fit variety. Some of his recommendations were very original and not always medical. The aspirant to health was advised, among other things, to wear "a skarlet nyhgt-cap" and to avoid all Scotsmen, who "youse flattering wordes and all ys falshode." However, his best-known book, the *Breviarie of Health*, contained very sound and much-needed advice on sanitation. Writing of "the pestilence," he said:

> This infirmitie doeth come eyther by the punishment of God, eyther els of a corrupt and contageous ayre, and one man infected with this sicknes may infect many men, this sicknes may come also with the stench of evill dirtie stretes, of Channelles not kept cleane, or standing puddles, and stinking waters, of seges, and stinking draughtes, of shedding of man's bloud, and of dead bodyes not deepely buryed, of a great company being in a little or small rome, or common pissing places, and of many such lyke contagiouss ayres.

Weights and Measures

One of the greatest scientists of the Renaissance was an Italian named Galileo. He is best known for his experiments in dropping objects from the top of the Leaning Tower of Pisa, and for his discovery of the spots on the sun. His value to medicine was his emphasis on the importance of measurement. He sought to make science exact, and apart from the telescope he constructed a variety of mechanical instruments including a barometer, a thermometer, and a 'pulsimeter,' or pulse-measurer.

Galileo taught at Padua, and a medical professor in the same

university adapted his ideas to the science of medicine. This was Sanctorius Sanctorius, who was responsible for the invention of the clinical thermometer and a pulse-clock. He also considered that the applications of the principles of weighing would reveal new knowledge about the human body, and with this in view he constructed a 'weighing-chair' attached to a balance. During a period of thirty years he spent much of his time in this chair, taking his meals there and even sleeping in it. He noted the changes in weight before and after eating and sleeping, making the discovery that the consumption of a pound of meat did not increase the weight of the body by the same amount. This he explained by what he called "invisible perspiration."

Sanctorius's experiments did not have much influence on the medicine of his time, but they led to the later researches in the study that we now call metabolism.

6

THE GREAT DISCOVERY

THE first known description of the circulation of the blood was made by the Chinese physician Hwang Ti, some twenty-six centuries B.C. It was surprisingly accurate so far as it went.

"All the blood in the body," it ran, "is under the control of the heart. The blood current flows continuously in a circle and never stops."

Hwang Ti said nothing about arteries or veins, and the way in which he arrived at his conclusion is unknown. He offered no explanation, and another four thousand years were to pass before the matter was finally resolved.

The Mysterious Movement of the Blood

Of all the problems that engaged the attention of physicians throughout the centuries none produced such a number and variety of theories as the study of the blood. It had been the subject of heated argument even in the days of Hippocrates, although he himself confessed that it was beyond him.

The blood was always on the move. The ancient Egyptians had found that out. It flowed through the heart—Hippocrates himself affirmed the fact. But why did it move? And how did it move? Where did it come from, and where did it go to? Were the veins the only vessels, or did the arteries also convey blood? Above all, what caused the blood to move? Was the heart the motive force, or might it be the liver? These were the questions that baffled the best brains for over two thousand years.

Aristotle had tried to answer some of the questions, but unfortunately he went wrong at the start by declaring that the arteries contained only air. In his opinion blood was carried only by the veins, and moved to and from the heart in a sort of ebb-and-flow motion.

Reference has already been made to the theories of the Alexandrian School. Hierophilus, it will be remembered, although adhering to the ebb-and-flow idea, asserted that the arteries contained both blood and air. His fellow professor, Erasistratus, denied this, but made amends by discovering the valves of the heart. He attributed the origin of the blood to the liver—an error that was to persist for many centuries.

By the dissections carried out by Hierophilus and Erasistratus something came to be known of the structure of the heart, about which a few words may now be said. It is a hollow muscular organ, divided down the middle by what is called a septum. Each side is further divided into two separate chambers, which have been named after other Latin words. The top one is called the auricle, on account of a resemblance to the ear of a dog, while the lower one is known as the ventricle, meaning 'little stomach.' There are thus four separate chambers in the heart. The valves discovered by Erasistratus are located on either side, between the auricle and the ventricle. Each auricle is fed by veins, and each ventricle leads into an artery.

The controversy was carried on until the appearance of Galen, who proceeded to settle it, as he thought, for ever. To begin with, he made short work of the theory that the arteries contained only air. He did this by a simple experiment on one of his animals. Isolating a section of an artery, he tied it off at each end so that neither blood nor air could enter. Then he cut the artery in the middle—and out came the blood.

Unfortunately Galen never thought of the idea of the blood going round in a circle, and he followed Erasistratus's error of regarding the liver as its point of origin. On the basis of these theories further mistakes were inevitable. He traced the blood from the right ventricle to the lungs, and rightly suggested that it was there freed of its impurities and charged with what he termed "vital spirit"—we call it oxygen. But so long as he clung to the ebb-and-flow idea it was impossible for him to understand the true function of the heart. He made a fundamental mistake in assuming that blood could pass from one side to the other, through the septum.

Galen worked out a complete theory of the blood-system to his own satisfaction, and to the satisfaction of doctors for the next thousand years. The controversy was, it seemed, finally settled.

New Ideas

Then came the Renaissance, and the whole question flared up again. Leonardo da Vinci was the first to cast doubts on the theory of Galen. He left some superb drawings of the heart, which he dissected and investigated at length. He proved that the valves discovered by Erasistratus were designed to permit one-way traffic only—from the auricle down to the ventricle—and he expressed grave doubts about the idea of the blood passing from one side of the heart to the other. These misgivings were reaffirmed in an ironical passage in Vesalius's *Fabrica*—"we are forced to wonder at the art of the Creator, by which the blood passes from right ventricle to left ventricle through pores which elude the sight." Later he was more emphatic. "I do not see," he wrote, "how even the smallest particle can be transferred from the right to the left ventricle through the septum."

This was a very important statement, for the whole of Galen's theory depended on a connexion between the two sides of the heart. A theory of Galen's could not be discarded so lightly, however, and other scientists began to wonder if the passage of blood might be achieved by an indirect route. It was this idea that led to the discovery of what is called the pulmonary circulation.

The Pulmonary Circulation

The pulmonary, or lesser, circulation is one of the simplest and most beautiful of all Nature's works. The blood leaves the right ventricle loaded with carbon dioxide drawn from all parts of the body. It courses along the pulmonary arteries to the lungs. There, through the process of breathing, the carbon dioxide is thrown off and oxygen taken in. Thus purified, the blood returns via the pulmonary veins to the left auricle of the

heart, ready to nourish the body again and collect more carbon dioxide.

Galen, as has been seen, discovered the first half of the process. The second half was discovered 1350 years after his death.

The discovery was made, apparently independently, by a Spaniard and an Italian. The former, Michael Servetus, described it perfectly. "The blood," he wrote, "is transmitted from the pulmonary artery to the pulmonary vein, by a lengthened passage through the lungs, in the course of which it becomes of a crimson colour." He explained the change in colour as the result of the removal of "fuliginous vapours" by the act of expiration, or breathing out.

The Italian, Realdus Columbus, was a colleague of Vesalius at Padua. He said much the same as Servetus, and added the final word to Vesalius's refutation of the Galenic theory of direct communication between the two sides of the heart.

Fresh Advances

Neither Servetus nor Columbus had much idea of what happened to the blood after it got back to the left auricle. Both agreed that the liver was the seat of origin, and neither disputed the old ebb-and-flow theory. In the same century, however, two other Italian scientists carried the matter nearer the truth.

Andreas Cesalpinus, a professor at Pisa, emphatically denied that the blood originated in the liver, and he made a very thorough study of the action of the heart. He observed that it contracted and dilated, or expanded, alternately, and he came to regard it as a sort of natural pump. When the heart dilated, he declared, blood from the veins poured into the auricles. The blood passed through the valves into the respective ventricles, and a muscular contraction forced it out into the arteries.

Cesalpinus was nearer to the truth than anyone before him, yet he failed to pursue his investigations to their logical conclusion. Although he knew the principle of the pulmonary circulation, he was content to accept the ebb-and-flow theory, and the rest of his work was of little value.

A similar attitude marred the work of Fabricius ab Acqua-

(1537- 1619)

pendente, who might be termed a 'grand-pupil' of Vesalius, his master having been taught by the great anatomist. He wrote a very valuable book on the valves of the veins—or "little doors," as he called them. He made the important point that the mouths of these valves were always directed towards the heart. He himself failed to grasp the significance of his own discovery; he still believed that the blood in the veins flowed towards the heart as well as away from it, and he put the function of the valves down to a safety-device to prevent the flow from the heart from being too rapid and violent.

But Fabricius had a pupil, who showed great interest in these valves. Some years later this pupil had a conversation with the famous chemist, Robert Boyle. Boyle asked his friend a question, and he considered the reply worthy of record:

> He answer'd me, that when he took notice that the Valves in the Veins of so many several Parts of the Body, were so Plac'd that they gave free passage to the Blood Towards the Heart, but oppos'd the passage of the Venal Blood the Contrary way: He was invited to imagine, that so Provident a Cause as Nature had not Plac'd so many Valves without Design: and no Design seem'd more probable, than That, since the Blood could not well, because of the interposing Valves, be sent by the Veins to the Limbs; it should be sent through the Arteries, and Return through the Veins, whose Valves did not oppose its course that way.

Boyle's question was how his friend first conceived the idea of the circulation of the blood. The friend, of course, was

William Harvey

Harvey was born at Folkestone, in 1578, and educated at Canterbury Grammar School. When fifteen years old he went to Cambridge University, took a degree in arts, and then set off to Padua to study medicine. He stayed there four years, studying under Fabricius, and graduated as a doctor of medicine. Then he returned to England to set up in practice in London. Five years later he had established himself as a Fellow of the College of Physicians and assistant physician to Bart's. In 1616 he was appointed Lumleian Lecturer of the college; and it was

in the course of his lectures there that he first revealed the discovery which Sir Thomas Browne rated as even greater than the discovery of America by Christopher Columbus.

Harvey's Method

If ever there was a true scientist it was William Harvey. To him nothing was valid until it had been proved by experiment. However certain a deduction might appear, it remained a theory until it had been practically demonstrated. Thus he delayed sixteen years after his appointment as Lumleian Lecturer before he made his discovery public.

Harvey tested every theory about the blood since the time of Aristotle, and exposed their fallacies one by one. In doing so he knew what to expect from his contemporaries. Even in the seventeenth century it was held to be presumptuous to cast doubts on the teachings of the ancients. His own theories he subjected to the severest tests of all, and deliberately withheld them from publication until his evidence was too convincing to be doubted.

Most of his experiments were based on dissection, mainly of animals. "I profess both to learn and to teach anatomy not from books but from dissections, not from the positions of philosophers but from the fabric of Nature." He dissected a variety of species, including dogs, pigs, serpents, slugs, oysters, and even wasps, as well as human beings. His passion for this work never deserted him, and later in his life, during a holiday in Europe, he wrote to a friend complaining that he "could scarce see a dogg, crow, kite, raven, or any bird or anything to anatomise."

His first and most significant experiment, however, did not involve dissection at all. It is still used as a demonstration of the movement of the blood, and it can be performed by any two persons without apparatus. The demonstrator selects a surface vein on his subject, usually on the arm. He then presses with his forefinger on a point near the wrist—that is, away from the heart. Next he runs the forefinger of his other hand along the vein, towards the elbow. Immediately the blue colour fades,

and the vein seems to disappear. This is simply because the blood has been pushed farther along the arm.

Now if the blood really ebbed and flowed along the veins, as was still the popular theory in Harvey's day, it would be reasonable to expect it to return to the vein from the direction of the elbow. But in actual fact this does not happen. The section of vein remains empty until the pressure near the wrist is released. Then it fills up again immediately, and the blue colour returns. In other words, the blood in the veins moves in only one direction: towards the heart. The ebb-and-flow theory, therefore, is false.

After satisfying himself that this was not peculiar to one vein, Harvey next set out to find if a similar one-way traffic occurred in the arteries. This was not quite so easy of experiment, because these blood-vessels are not so near the surface as the veins. He therefore repeated Galen's experiment on an animal—exposed a section of artery, tied it off at both ends with ligatures, and made an incision in the middle. Galen had been concerned only with proving that the arteries contained blood; Harvey took it a good deal further. When the section of artery was empty he removed the ligature farthest from the heart. Nothing happened. No fresh blood flowed into the artery. The ligature was replaced, and the other one removed—the one nearer the heart. Immediately the blood started pulsating into the artery.

Harvey took stock. The blood in the veins moved in one direction only—towards the heart. The blood in the arteries moved only away from the heart. The flow was continuous. The blood in the veins had to come from somewhere. The blood in the arteries had to go somewhere. In the heart itself the pulmonary circulation had established the connexion between the right ventricle and the left auricle. The right auricle was fed by blood from a large vein. The left ventricle pumped blood into a large artery. Therefore—

But Harvey did not jump to conclusions, however obvious. He turned his attention to the workings of the heart. Although on the eve of one of the very greatest discoveries in medicine, he found this a fascinating subject. The action of the organ, he

said, "is accomplished in the twinkling of an eye, coming and going like a flash of lightning." He found that the average number of contractions and dilations was seventy-two per minute—and incidentally discovered the source of the pulse in the artery of the wrist, to which Galen had attached so much clinical importance without ever realizing its true meaning.

Finally Harvey was satisfied. The blood, he decided, moved in a circle. It travelled from the left ventricle to the arteries, thence to all parts of the body; then it returned via the veins to the right auricle. That was the systemic, or greater, circulation. From the right auricle the blood went through the valves into the ventricle, whence the pulmonary circulation began. From the pulmonary arteries it passed into the lungs, returning through the pulmonary veins to the left auricle. It was then sent down to the left ventricle—and it was back at the beginning again. The valves in the veins ensured a one-way traffic—and truly, as Harvey told Boyle, "so Provident a Cause as Nature had not Plac'd so many Valves without Design."

In 1628 Harvey published his discovery in his famous book, *De Motu Cordis et Sanguinis*, or *On the Movement of the Heart and Blood*. It was dedicated to King Charles I, whose relation to the kingdom Harvey neatly compared with the relation of the heart to the human body. This book was nothing short of a complete denial of one of the most cherished theories in medicine, and Harvey knew in advance that he was in for a bad Press. He said as much in the book:

> What remains to be said upon the quantity and source of the blood which thus passes, is of so novel and unheard-of character, that I not only fear injury to myself from the envy of a few, but I tremble lest I have mankind at large for my enemies, so much doth wont and custom, that become as another nature, and doctrine that once hath struck deep root, and respect for antiquity influence all men: still the die is cast, and my trust is in my love of truth, and the candour that inheres in cultivated minds.

Harvey had not overestimated the animosity that greets anyone committing the sin of being original. He was immedi-

ately attacked from all quarters, and "he fell mightily in his practice and 'twas believed by the vulgar that he was crack brained." He endured the criticism with calm and restraint, still trusting to "the candour that inheres in cultivated minds." But it was the solid mass of evidence he had toiled to produce that won him the day. The storm died down, and although some opposition persisted, he lived to see his discovery accepted and finally acclaimed.

The Man himself

"He was not tall, but of the lowest stature, round-faced, olivaster-complexion; little eie, round, very black, full of spirit; his haire was black as a raven, but quite white twenty years before he died."

Such is the best description we have of this pioneer of modern medicine. In character Harvey was reputed to be quick-tempered, but his writings give no indication of this. He was certainly absent-minded. At the famous Battle of Edgehill, where he was in professional attendance on Prince Charles and the Duke of York, he so far forgot himself as to settle down under a hedge and "tooke out of his pockett a book and read." He did not read for long; "a bullet of a great gun grazed on the ground neare him, which made him remove his station."

Harvey was appointed physician extraordinary to James I in 1618, and it is interesting to note that seven years later he was under suspicion of having murdered his King by poisoning. Charles I obviously believed him innocent, for he not only appointed him court physician, but took a keen personal interest in the scientist's researches. Harvey suffered later for his association with the ill-fated King, and he spoke bitterly of an occasion when a gang of rioters broke into his lodgings in Whitehall and "not only stripped my house of all its furniture, but, what is a subject of far greater regret to me, my enemies abstracted from my museum the fruits of many years of toil."

Harvey made several other notable contributions to medical science, and he was elected President of the College of Physicians. His health did not allow him to accept this honour, although

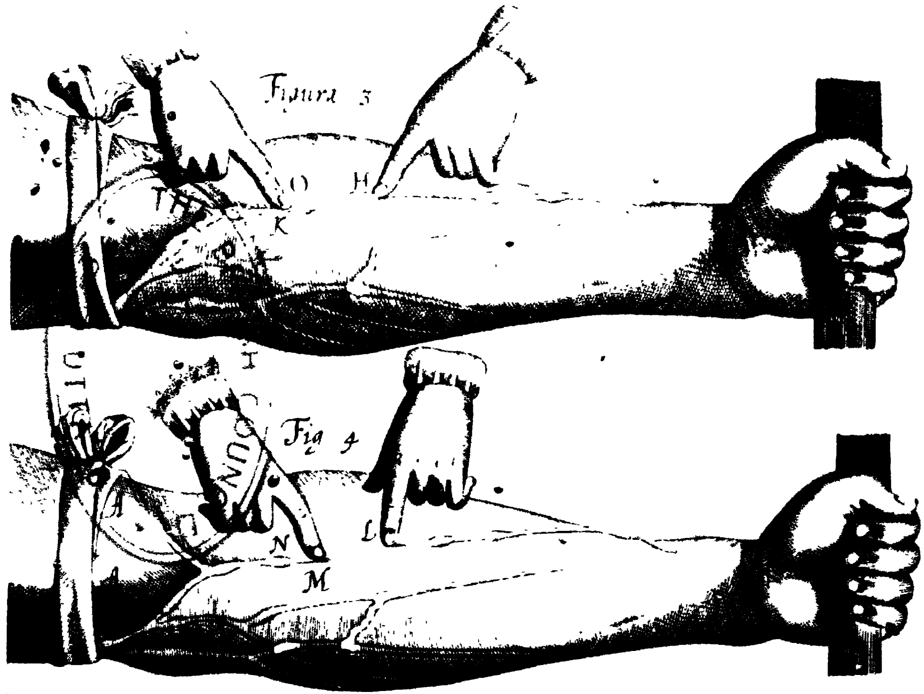
he continued his Lumleian Lectures almost to the end of his life. One of his last actions was to donate a library and museum to the college, together with a large number of his own priceless specimens. He died in 1657, at the age of seventy-nine.

Completion of the Work

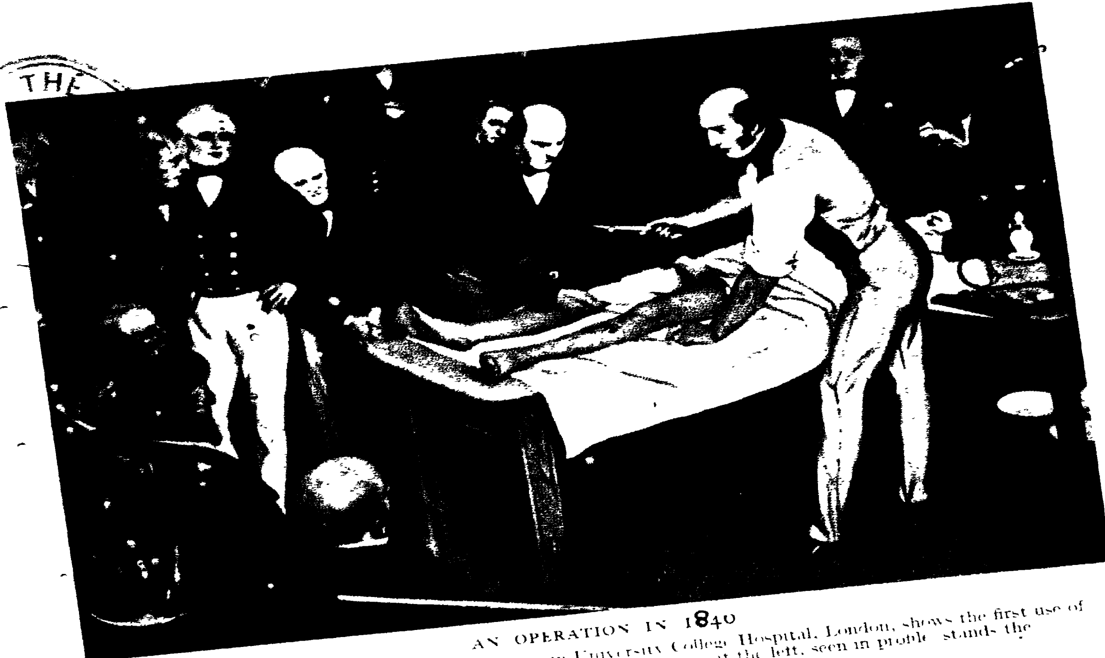
There was one missing link in the chain of Harvey's discoveries. He showed how the blood went from the heart to the arteries, and how it eventually returned to the heart through the veins; but how did it pass from the arteries to the veins? Harvey had an inkling, but the question could be answered only with a microscope. Had such an instrument been available, he could scarcely have failed to complete the discovery himself. Actually this work was done only four years after his death, by an Italian named Marcello Malpighi, who observed in the lung of a frog the tiny blood-vessels known as capillaries.

The word 'capillary' means 'hair-like.' Capillaries are the smallest and most numerous of the blood-vessels, and form a delicate network linking the arteries to the veins. It is through the capillaries that the precious oxygen and nourishment are given to the tissues of the body, in exchange for the carbon dioxide that is finally thrown off by the action of the lungs.

Harvey's aim was to discover the nature of the movement of the blood, and this he fully achieved. He did not pretend to know the function of the blood in its course round the body. He regarded this as another problem, and frankly admitted that his own discoveries threw no light on the question. "Whether for the sake of nourishment or for the communication of heat is not certain," he wrote, and was content to leave it to others to find out.



HARVEY'S EXPERIMENTS ON VEINS



AN OPERATION IN 1840

The illustration, which is taken from a painting in University College Hospital, London, shows the first use of ether anaesthesia in Britain. The surgeon is Robert Liston; at the left, seen in profile, stands the student Joseph Lister.

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7

TWO CENTURIES OF PROGRESS

THE great discoveries of the Renaissance changed the whole basis of medical science. Medical practice, however, was but slowly affected. The new conceptions of anatomy and physiology were not immediately translated into terms of diagnosis and treatment. The work of Vesalius and Harvey attracted the attention of philosophers as well as scientists, and a number of different 'schools of thought' sprang up—somewhat similar to the sects that had pervaded Greek medicine after the death of Hippocrates. Ingenious theories were propounded, and medicine became the subject of many long treatises and learned arguments that ignored the question of practice altogether.

This did not help the people who were ill. The majority of general practitioners were of the old school, and their treatment was still characterized by an over-dosage of drugs, for the most part useless, rather than rational methods. Furthermore, superstition was still rife, witches were generally believed in, and few of the common people dared to scoff at the powers of charms and incantations. Clinical medicine badly needed a reformer.

The "English Hippocrates"

The reformer was born in 1624, and his name was Thomas Sydenham. His reformation was not so much a new advance in method as a long-needed return to the teachings of Hippocrates. For although doctors all paid lip-service to the Father of Medicine, his principles were almost entirely neglected.

Sydenham was born at Wynford Eagle, in Dorsetshire. His family was strongly Puritan in sympathy, his father and four brothers all being officers in Cromwell's army. Thomas joined them at the age of eighteen, and not until four years later could

Sydenham himself defined disease as "no more than a vigorous effort of Nature to throw off the morbific matter, and thus restore the patient." As in the Hippocratic doctrine, the physician should never consider himself as any more than Nature's assistant.

He did not despise the use of drugs, however. If a drug showed itself to be consistently effective in the treatment of a certain disease, he took it into regular use and advised other doctors to do the same. To-day we call such drugs 'specifics,' and the one with which Sydenham's name is always associated is cinchona bark, used in cases of malaria. He also prescribed iron for the treatment of anæmia, and made the first preparation of tincture of opium.

In 1666 Sydenham published his famous book *The Method of Treating Fevers*. In this work were the results of years of meticulous observation, described in a clear and vivid style that could be compared only with the case-histories of Hippocrates. Sydenham defined a fever as "Nature's engine which she brings into the field to remove her enemy." Included in the book was the first known description of scarlet fever—the name itself was Sydenham's. In another work he wrote on gout, about which he was especially qualified to speak as he had suffered from it continually since the age of thirty.

The study of medicine, said Sydenham, was the study of disease. While he fully recognized the importance to the physicians of a knowledge of anatomy and physiology, yet these by themselves were useless. Not from books and lectures alone could the student hope to acquire all his knowledge; as Ambroise Paré had said about surgery, the best teacher was experience.

On one occasion Sydenham expounded this principle with more force than tact. A young man, Sir Hans Sloane, was sent to him with a letter of introduction in which he was put forward as "a ripe scholar, a good botanist, and a skilful anatomist." The physician read the letter and then handed it back to its bearer. "This is all very fine," he said, "but it won't do. Anatomy, botany—nonsense! Sir, I know an old woman in Covent Garden who understands botany better, and as for

anatomy, my butcher can dissect a joint full as well. No, young man, all this is stuff. You must go to the bedside, it is there alone you can learn disease!"

Similar advice is given to medical students to-day.

Every good doctor is a good psychologist, and Sydenham was no exception. A very good story is told of his novel treatment of a persistent patient in whom he could find no evident disease. After wasting a lot of time on this man Sydenham at last told him frankly that he could do no more. However, he added, a colleague of his, one Dr Robinson, might be able to succeed where he had failed, if the patient cared to visit him. The patient was only too pleased, despite the fact that Dr Robinson lived as far away as Inverness. Sydenham therefore wrote a case-history and a letter to his colleague, and with these documents the patient set off.

He reappeared in London some weeks later, and looked anything but pleased when he presented himself at Sydenham's house. He had gone all the way to Inverness, he said, only to find that no Dr Robinson existed. He had sought for him everywhere, even interrogated the oldest inhabitant, who denied all knowledge of such a person. Sydenham listened to his patient's recital without interrupting. Then, when it was finished, he said quietly, "But you are in much better health." The patient's anger rose. He looked and felt well, and could not deny it; but he was not going to let Sydenham take the credit. "No thanks to you," he retorted. "No," agreed the physician blandly, "it was 'Dr Robinson' who cured you. I wished to send you a journey with some object and interest in view; in going, you had Dr Robinson and his wonderful cures in contemplation; and in returning, you were equally engaged in thinking of scolding me!"

New Medical Centres

The only countries that had been in any way prepared for the Renaissance were Italy and France. Their medical schools were well established by the fifteenth century, and they thus had a good start on the rest of Europe. They kept their supremacy

until the seventeenth century, by which time Padua was universally recognized as the medical centre of the world.

The first serious rival to this town was Leyden, in Holland. Here an entirely new form of teaching was introduced, with such success that the school eventually replaced Padua as the centre of medicine in Europe. In the Italian and French schools instruction had consisted almost entirely of lectures by professors on anatomy and physiology, with some theoretical study of disease. The school of Leyden changed this completely by the introduction of clinical teaching. The students were brought into contact with actual cases, and learned diagnosis and treatment at first hand.

The greatest exponent of this method was Hermann Boerhaave, who was appointed a professor at Leyden in 1701. Probably the finest clinical teacher of the eighteenth century, he brought the wisdom of Hippocrates to the lecture-room, and encouraged his pupils to observe living patients as well as to study skeletons. He was allowed twelve beds as a demonstration ward, and when a patient died he took his students to the dissecting-room to attend the post-mortem examination.

Devoted as he was to clinical teaching, Boerhaave did not neglect the other branches of medical instruction. He sought to bridge the gulf between science and practice rather than to widen it. He made original contributions to chemistry, and edited a collection of the works of Vesalius—his reputation as an anatomist was especially high. But he did not teach anatomy, or any other branch of medicine, as a self-contained science. He sought to unify teaching, bringing every subject into line with a single idea: application to medical practice. He did not waste his time on academic arguments and theories. He wanted to produce practising doctors, not philosophers. With Boerhaave, as with Hippocrates, the patient always came first, and only from observation of the patient could one acquire a knowledge of disease. Much of this teaching is strongly reminiscent of Thomas Sydenham, and there is no reason to doubt the story that Boerhaave always used to raise his hat when he mentioned the name of the English physician during his lectures.

So famous did Boerhaave become that students flocked to Leyden from all parts of Europe. The city had to extend its walls to accommodate them, it was said. And when a Chinese mandarin addressed a letter simply to "Dr Boerhaave, Europe," it was duly delivered.

The influence of Leyden made itself felt all over the continent, and it played a part in the foundation of at least two new medical schools. One of these was at Vienna, and was established by another Dutchman, Gerhard van Smieten. A pupil of Boerhaave, he became a teacher at Leyden and was even suggested as the great professor's successor. He did not gain this appointment, however, and went instead to Vienna as physician to the Empress Maria Theresa. He found in the town a medical school of sorts, badly in need of reformation. Using the influence his official position gave him, he reorganized the school completely, introducing the general principles on which the Leyden school was based. Thanks to Smieten's efforts, Vienna eventually became one of the leading medical centres in Europe.

The other school indebted to Leyden was Edinburgh, which was destined to supplant the Dutch city itself as the centre of European medicine. The Royal College of Physicians, Edinburgh, was founded in 1681. Four years later three physicians were appointed to the town, two of them being graduates of Leyden. The third, Archibald Pitcairn, did not go to Leyden until he was forty years of age—and then it was as a professor, not a student. He played a considerable part, however, in the foundation of the famous Edinburgh school, which produced so many of the great doctors of the nineteenth century. It was he who first introduced anatomy to the city, and he fought a strenuous campaign against the division of teachers into sects. The duty of the physician, he said, was "to apply himself to discover by experience the effects of medicines and diseases." The emphasis, as was shown in his teachings, was on the word 'experience.'

The spirit of Leyden was kept alive in Edinburgh by three successive professors of anatomy—Alexander Monro, Alexander Monro, and Alexander Monro. The first two Monros studied

at Leyden, and Grandfather Alexander obtained his Edinburgh appointment at the age of twenty-two. He kept it for thirty-six years, at the end of which he was succeeded by his son. The latter, who was considered an even greater teacher than his father, held the post for forty years, when Alexander the third took over and carried the total family score to well over a century.

The Great Plague

In the middle of this period of enlightenment and progress something like twenty per cent. of the population of London was wiped out by a single disease. This was the Great Plague of 1665.

There is an obvious temptation for the cynic to ask just how the common people had benefited from the medical discoveries and teachings that followed the Renaissance. Hardly at all, is the answer—so far as the prevention of plague was concerned. But let the cynic turn his attention to an epidemic of a later age, when medical science was far more advanced. In 1918 over 13,000 died in London from influenza—and London was by no means the most affected. The total mortality of this epidemic reached the staggering figure of twenty-one millions.

A similar epidemic was expected twenty-nine years later, but happily it did not come. Had it done so, it would have been nothing like so bad as the epidemic of 1918. The research of scientists had led to the preparation of an anti-flu vaccine, stocks of which are held in centres all over the country, in readiness for any epidemic that may break out. Yet we do not blame the medical profession for what happened in 1918. Have we any right, therefore, to sneer at the failure of seventeenth-century doctors to prevent the spread of the Great Plague?

The bacillus of plague lives in the stomach of a flea. The flea makes its home on the body of a rat. Had an attack been made on London rats, the Plague might never have been called "Great." But in 1665 no one thought about the rats. True, it was suggested that the disease might be spread by animals, but

the guilt was ascribed to dogs, large numbers of which therefore lost their lives for no good reason.

"Bring out your dead! Bring out your dead!" was the commonest street-cry in the summer of 1665. There was no time for funerals or even separate burials, and certainly not enough wood for coffins. The dead were buried in pits, and the living fled from London for their lives—and thus spread the disease to other parts of the country. To anyone living in those days it must have seemed as if the whole population of England might be completely wiped out. But towards the end of the year the mortality decreased; and in the following year most of the rats and their fleas were killed by the Great Fire.

The plague was no respecter of persons. Daniel Defoe, in his *Journal of the Plague Year*, records that it "defied all medicines, the very physicians were seized with it, with their prescriptions in their mouths." There have been many great triumphs in the history of medicine; let homage also be paid to the failure of those gallant doctors who remained at their posts throughout the epidemic, risking and often losing their lives in the hopeless task of trying to save the afflicted.

Over two hundred years after the Great Plague the bacillus was discovered in an epidemic in Hong Kong by Alexandre Yersin, a pupil of Pasteur, and a Japanese scientist named Kitasato. The origin of the disease was established as the rat-flea, and preventive measures were taken. Then, in 1896, another of Pasteur's pupils, W. M. F. Haffkine, succeeded in preparing an anti-plague vaccine. To test his vaccine he chose the most certain and most dangerous way: he injected it into his own body. Within a matter of hours his temperature had risen to 102°, and he began to experience the symptoms he knew so well. But the vaccine proved to be safe; Haffkine recovered, and lived to see thousands of lives saved by his work.

Surgery and the Hunter Brothers

The surgeons, it will be remembered, did not succeed in finally breaking away from the barbers until 1745. Well before that date, however, the practice of surgery had been recognized

as a vital branch of medicine, if not actually as a profession in its own right.

One of the men mainly responsible for the passing of the Act of 1745 was William Cheselden. Born in 1688, he joined the Company of Barber-Surgeons as a young man, but soon began to chafe against the limitations imposed. Realizing the total dependence of surgical practice on the study of anatomy, he supplemented the inadequate training given by the Masters of the company, and began to give lectures and demonstrations on his own account. In 1712 he was elected a Fellow of the Royal Society—a very high honour for a barber-surgeon. A year later he published his first book, *The Anatomy of the Human Body*, and in 1718 he was appointed surgeon to St Thomas's Hospital.

Cheselden's greatest achievement was in the historic operation of lithotomy, or removal of a stone from the bladder. Although quite a common operation, it had an ugly record of mortality, and even when successful it caused intense pain to the patient. Cheselden introduced a brand-new technique, cut the mortality down to seventeen per cent.—and reduced the time of the operation to no more than fifty-four seconds!

After Cheselden came Percival Pott, who had both a disease and a fracture named after him. The latter is the common fracture of the lower end of the fibula. Pott's own personal fracture, however, was of the tibia, incurred as a result of a throw from his horse in the Old Kent Road. From this accident he gained valuable knowledge that would otherwise have been denied him; but apparently he came to regard the fracture as literally too near the bone, for he spent his convalescence writing a book on hernia.

Pott also was elected a Fellow of the Royal Society, and he spent forty-two years as surgeon to St Bartholomew's. He wrote various treatises, notably on diseases of the eye and head-injuries. Cheselden and Pott together were responsible for raising surgery to a standard that compelled physicians to revise their traditional attitude of superiority. Meanwhile, however, a twenty-two-year-old Glaswegian had come to London, and the teaching of surgery was soon to reach new heights.

William Hunter studied at Edinburgh University, where he was fortunate enough to learn anatomy under the first Alexander Monro. When he arrived in London he became a pupil of another Scot, William Smellie, who was already famous as an obstetrician. Hunter's interest remained in anatomy, and after a visit to Leyden he opened a private school in London. In 1748 he was joined by his younger brother, John, who had just lost his job as a cabinet-maker's apprentice. He soon proved his worth as a practical anatomist, however, and William set him to learn surgery first under Cheselden and then under Pott. William himself, meanwhile, was preparing to qualify as a physician.

After a few years John went with the British Army to Portugal, and had four years' experience of war surgery. He was thirty-five when he came back to England and found his brother appointed physician extraordinary to the Queen. John returned to the teaching of anatomy. It is recorded that he was not such a good lecturer as his older brother, but at least he had a sense of humour. On one occasion he found a class of one solitary pupil awaiting him; as he entered the room, it occurred to him that he would be unable to begin with the traditional "Gentlemen"—so he sent the attendant for a skeleton, and thus was able to open his lecture in the usual way!

By now it was clear which was the greater of the two brothers. William was a good surgeon, a good physician, and a competent teacher; John was a scientist, a tireless experimenter (he rarely allowed himself more than a few hours' sleep a night), and one of the greatest anatomists since Vesalius. Like Harvey, he never tired of dissection. He is said to have dissected five hundred different species of animals, including bees, mice, lizards, stags, leopards, and even whales! For the body of a giant of an Irishman he paid no less than £500. He built a museum for his specimens, which eventually numbered over 13,000.

Although surgery was his profession John Hunter never regarded operative treatment as anything but a regrettable necessity. "To perform an operation is to mutilate the patient whom we are unable to cure," he said. "It should therefore

be considered as an acknowledgment of the imperfection of our art." It was only natural, therefore, that he should share his brother's attitude to the inter-dependence of surgery and medicine, and he himself conducted a series of investigations on venereal disease. In one of these he deliberately inoculated himself with syphilis, an heroic action which led to his death in 1773.

The Principle of Percussion

One of the most important discoveries of the eighteenth century was made by a Viennese physician named Leopold Auenbrugger. He was born at Graz in 1722, the son of an innkeeper. Leopold used to help his father in the inn, and one of the jobs he was given was to find out the levels of the wine in the wooden casks in the cellar. His father had shown him how to do this: you just rapped on the cask with your knuckles, and the sound told you the rest. A resonant note signified only air, which meant you were above the level; a duller sound indicated the presence of wine.

Leopold did not follow in his father's footsteps, however. The innkeeper had higher ambitions for his son, and chose the medical profession for his career. The young man studied at a medical school, passed his examinations, and set up in practice. He was a competent doctor, but apparently nothing more. However, he was very fond of music. He played the flute, and wrote the libretti of an opera called *The Chimney Sweep*.

Perhaps the reader may be asking what these biographical details have to do with the history of medicine. Let it be said now, then, that had not Auenbrugger rapped his father's wine-casks and played the flute, his name might never have found a place in medical history at all.

One of his patients died. The physician conducted a post-mortem examination, and found that the lungs were filled with fluid. "Had I known that," he said regretfully, "I might have saved his life." But regrets do not make a doctor. The man was dead; other patients of his, still alive, might also have fluid in

their lungs. If he could find that out now, then he really might save some lives.

Brooding on the problem, Auenbrugger suddenly recollected his father's wine-casks. The contents of these casks, he remembered, could be discovered by the simple method of tapping and listening. Fluid and air could be distinguished from each other by the degree of resonance in the sound. (This was where his ear for music came in.) Now a wooden cask is not unlike the human chest. The contents of each are protected by a strong barrier, and are thus completely hidden from view. Might not the contents of the chest, then, be revealed in a similar manner—by tapping and listening?

Auenbrugger tried it out. He surprised his patients by tapping their chests and listening—and the results exceeded his wildest hopes. The differences in sound were as clear as they had been with the wine-casks. Diagnosis was given an invaluable new aid, which was eventually to become a routine in any chest-examination. To-day doctors tap and listen as much as ever, and the method has been given the name of 'percussion'—from the Latin word meaning 'to strike.'

For seven years Auenbrugger used this method of examining the chests of his own patients. Then, satisfied as to its efficacy, he gave his discovery to humanity in a small book entitled *Inventum Novum*, or *New Invention*, published in 1761. His opening sentence now reads like a platitude:

"The chest of a human being, when struck, makes a sound."

Auenbrugger had read some medical history, and he did not expect his discovery to be readily accepted. "I have not been unconscious," he wrote, "of the dangers I must encounter; since it has always been the fate of those who illustrated or improved the arts and sciences by their discoveries, to be beset by envy, malice, hatred, detraction, and calumny."

To his surprise and, no doubt, mortification, he was beset by none of these things. He was simply ignored. The book was scarcely noticed by the medical profession, and it was not until fifty years later that its tremendous importance was realized. Then it was a Frenchman, Jean Nicholas Corvisart, Napoleon's

private physician, who was responsible. Coming across a copy of Auenbrugger's forgotten book, he was so impressed that he translated it into his own language and recommended the general adoption of this "beautiful invention," for which he paid Auenbrugger full credit. As Corvisart was the most influential medical man in France, percussion quickly came into general use in that country. Auenbrugger died in 1809, a year after Corvisart's translation, and had the comfort of seeing his discovery appreciated at last.

Seven years later an even greater discovery was made.

The Invention of the Stethoscope

It would be difficult nowadays to imagine a doctor without a stethoscope, yet its history dates only from the beginning of the last century. And for once the whole credit for the invention is due to a single man.

René Theophile Hyacinthe Laënnec was born of poor parents in Brittany in 1781. He was a thin, sickly child, nor did his physique improve as he grew up. As a man he measured five feet three—and was thin for his height! In spite of his natural disadvantages and his early poverty, however, he set his heart on medicine as a career, and began his studies in the hospital at Nantes. At the age of nineteen he went to Paris, where he had the good fortune to study under one of the very first heart-specialists—Jean Nicholas Corvisart. One can imagine that Laënnec soon knew all about the principle of percussion.

Laënnec proved a good doctor, and at the age of thirty-five he was appointed physician to the Necker Hospital in Paris. The majority of his cases there were consumptives, and he was beset by the usual difficulties in diagnosing diseases of the chest. The problem was brought home to him very forcibly on an occasion when his patient, a woman suffering from heart-disease, was too fat for the sounds of her heart to be audible. It was then that he had his great inspiration.

It has just been said the credit for the stethoscope is due to Laënnec alone. It would, however, be unfair to overlook the contribution—albeit unconscious—of two children who used to play

in the gardens of the Louvre. Their game was neither exciting nor original; one of them tapped and scratched at one end of a piece of timber, while his companion placed his ear to the other end and listened to the sounds. Laënnec was taking a walk in the gardens, and these youngsters caught his eye. He stopped and watched, and an idea was born. Returning to the hospital, he took up a small paper-covered book, tightly rolled it into a cylinder, and placed one end against the chest of his stout patient. To the other end of the cylinder he applied his ear, and had the privilege of being the first known human being ever to have an indirect audition of the sounds of the heart.

Now the principle behind the use of the stethoscope is known technically as auscultation, from the Latin word meaning 'to listen.' It was not a new method; accounts of its use for the detection of air or fluids in the cavities of the chest were left by the Greek physicians. But they and their successors for over twenty centuries had to rely on the unsatisfactory practice of placing the ear on the patient's chest. By localization Laënnec brought the sounds to the ear with a distinctness that could not otherwise be obtained.

Rolling up paper books was a method with obvious scope for improvement, and Laënnec set to work to construct a more convenient article. He adopted the same raw material that the children had used in their game, and the first stethoscope was a wooden cylinder, hollow in the middle, shaped like a funnel at one end. This form was used unchanged for several years, until an American doctor, Austin Flint, introduced the type known as 'binaural'—*i.e.*, leading to both ears—with the consequent exclusion of all other sounds. Wood was replaced by rubber, and with slight modifications this type is the one that is in general use to-day.

Acceptance of Laënnec's 'baton,' as he called it, followed fairly quickly, despite the usual opposition to novelty which greets every invention in every science in every age. Its importance was tremendous. It cleared the way for investigations that had never before been possible, and Laënnec started on these straight away. The information he obtained threw a new

light on diseases of the chest, and his book on the subject became a medical classic. The story of the stethoscope has found its way into general literature, in the delightful *Marlake Witches*, by Rudyard Kipling, who estimated that it had "saved hundreds, thousands, perhaps millions of lives." Of more weight was the striking tribute paid by Sir William Osler, who placed Laënnec's work among the "eight or ten greatest contributions to the science of medicine."

The greatest value of the stethoscope was in the diagnosis of tuberculosis, the study of which formed much of the inventor's later work. The end of his story is sad; for he died at the early age of forty-five, a victim of this very disease.

AN OPERATION IN 1946

Photo Paul opper

WILLIAM HARVEY

ANTONY VAN LEEWENHOEK

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THE STORY OF VACCINATION

AN outbreak of smallpox in England to-day is front-page news. In the century before the last some 40,000 people in this country died of it every year—and that figure is nothing compared with the numbers that lost their sight or were disfigured for life. It was so prevalent that Thomas Sydenham formed the opinion that its cause must be constitutional—"a desire the blood hath to change its state." The rest of Europe suffered similarly: In Russia alone in one year the mortality reached the fantastic total of two million. And Europe, it may be added, got off comparatively lightly. In Asia and Africa the disease wiped out whole tribes at a time.

There was no known cure for it. Once an epidemic broke out there seemed no means of prevention against it. There was only one consolation, and that was a small one: if a person survived one attack he was not likely to catch it again.

Now this fact must have been known ever since smallpox first began. No one knew why it was so, but that did not stop the very earliest doctors in history from trying to turn the knowledge to good account. Smallpox was sometimes fatal, sometimes serious, sometimes mild. In its mild form it was anything but pleasant, but at least the sufferer had the comforting knowledge that he was unlikely ever to experience anything worse. The dangers of contracting the disease were so great that a mild case was envied by people who had so far escaped altogether. From envy to emulation was an obvious step, and thus began man's first attempts at protective inoculation. The principle of immunity was put into practice long before it was first preached.

No single person or community can be credited with being the first in this field. It was the sort of thing that occurred independently to a lot of different people in different parts of

the world. There are records of this sort of inoculation having been practised among the early Hindus, Chinese, North Africans, and various other people at different periods in their history. Avicenna, for one, is known to have used it. From existing records, however, it seems to have been almost unknown in Europe until early in the eighteenth century, when it was introduced to England by Lady Mary Wortley Montagu. This lady, who holds a distinguished place in the history of literature, accompanied her husband to Turkey, and it was from Constantinople that she wrote the letter that was to gain her a place in the history of medicine.

> The smallpox [she wrote], so fatal and so general among us, is here entirely harmless by the invention of ingrafting, which is the term they give it. . . . They make parties for this purpose, and when they are met (commonly fifteen or sixteen together) an old woman comes with a nut-shell full of the matter of the best sort of smallpox, and asks what vein you are pleased to have open. She immediately rips open that you offer to her with a large needle (which gives no more pain than a common scratch) and puts into the vein as much venom as can lie upon the head of a needle, and after binds up the little wound with a hollow bit of shell, and in this manner opens four or five veins.

The "best sort of smallpox" was presumably the least virulent, for the resultant fever, said Lady Mary, was invariably mild, and she had found no record of any fatal consequences. She ended her letter by saying that she was so impressed that she intended to try the method on her little son.

A year later she did so, and the boy suffered no ill effects. Lady Mary was a person of some consequence in England, and her report attracted great attention. The medical profession was for a long time divided on the subject, but public opinion was emphatic. In 1722 the Princess of Wales had two of her children inoculated, and after that there was no stopping it. Eventually the College of Physicians gave it their formal blessing—and within a few years its counterpart in Paris solemnly condemned the practice. The French had good reasons for this. Although the inoculation saved a good many individual lives,

it caused a greater number of deaths among the community as a whole. There was no effective quarantine system, so inoculation had the inevitable effect of starting off fresh epidemics. As the disease had a habit of getting stronger as it was passed on, the death-rate went up instead of down. In 1802 a Dr Lettson reported to Parliament that since the introduction of the practice in England the smallpox death-roll had risen from seventy-two to eighty-nine per thousand.

But by 1802 vaccination had been discovered.

The Country Doctor

Edward Jenner was born in 1749, in the village of Berkeley, Gloucestershire. His first experience of inoculation against smallpox was strictly personal. The practice was at the peak of its popularity, and young Edward was duly 'ingrafted,' as the Turks would have put it. His childhood was otherwise undistinguished except for a quickly developed love of nature which was never to leave him. Born and bred in the country, he was a countryman all his life. Natural history especially interested him, and he soon began to acquire a large collection of fossils and birds' eggs.

Edward's father was vicar of the village, and after the boy had received a preliminary education he was sent to learn medicine under a Dr Ludlow at Sodbury, near Bristol. From there he journeyed to London, and at the age of twenty-one he began to study under the great John Hunter. The famous surgeon was his teacher for two years, by the end of which the pair had formed a close friendship.

After qualifying as a doctor Jenner returned to his native Berkeley to set up in practice. Now that his studies were completed he devoted his leisure hours to his old love of natural history. Hunter, with whom he was corresponding regularly, encouraged Jenner in this, and suggested a number of experiments he might carry out. One of the subjects that interested them both concerned the hibernation of hedgehogs. Jenner told his former master his own opinion, and received a reply that was later to encourage him to an experiment of a very

different nature. "Why think?" asked Hunter gently. "Why not try the experiment?"

Five years after his return to Berkeley Jenner married. He had now established a fairly large practice, and had no other desire than to spend the rest of his life in the village he loved. He was a good doctor, and popular in every class of society; and he played a leading part in forming a local medical association. He acquired a high reputation, as much as naturalist as a physician, and had several offers of town and oversea appointments, which would have been far more lucrative than his country practice could ever become. He was not tempted. Although he had little worldly ambition, however, he had an active and inquiring mind. In addition to his nature studies he occupied himself with some private researches in medicine and pharmacy. At the same time, quietly and methodically, he was studying a disease common among cows.

Cowpox and Smallpox

Jenner's interest in this subject was first aroused when he was still a student, even before he went to London. While in Dr Ludlow's house in Sodbury he heard a chance remark that was to haunt him for over twenty years. The conversation was about smallpox—a topic as common as the weather in those days; and a milkmaid who happened to be present remarked carelessly:

"I cannot take that disease, for I have had the cowpox."

The young student made no comment, but the remark set him thinking deeply. He had no opportunities then to do much more than think, but while in London he mentioned the incident to John Hunter. It was not in the anatomist's line, of course, but he showed interest and encouraged Jenner to see if he could find out more about it.

When Jenner returned to Berkeley and started as a general practitioner, therefore, he set out to discover what truth there might be in the milkmaid's remark. Inquiry revealed that it was based on a popular belief in the neighbourhood that smallpox never attacked a person who previously had had cowpox. Jenner mentioned this to other doctors, but they showed little

interest in the legend. Country people were full of superstitions and absurd beliefs, and they were especially notorious for their weird and wonderful 'cures' for diseases. There seemed no reason to suppose that this story might be any more credible than the others.

Jenner was not so sure, and he began to study cows. The disease to which the milkmaid referred normally manifests itself in the form of spots or pustules on the udders of the animals. It is contracted by human beings as a result of contact with the infected udders, usually during milking. The disease is trivial in humans; apart from a few spots or sores on the hands, the sufferer hardly notices it. Even in its severest form there is little danger of death or even disfigurement.

If, thought Jenner, this infection could really prevent smallpox, why could it not be substituted for the dangerous inoculation that was then in use?

As a doctor he was regularly called on to administer the ordinary smallpox inoculations, and his observant mind noticed something that made him certain that the peasants were right. The inoculations sometimes failed to 'take,' and no symptoms of smallpox developed at all. When this happened Jenner asked the person concerned if he or she had ever had cowpox. The answer was nearly always in the affirmative.

Jenner continued his observations, until they were unfortunately suspended by a temporary disappearance of cowpox in the district. The disease came back, though, and he resumed his work of going round examining cows and questioning milkmaids. He was becoming more and more certain, and he began to expound his suggestion of cowpox inoculation to his colleagues. They were not impressed. For one thing, it was hardly the place of a country doctor to make discoveries; and, anyway, the medical profession ought to hold itself aloof from the superstitions of ignorant peasants. When Jenner brought the subject into lectures he gave at the local medical society he was actually threatened with expulsion if he did not keep his ridiculous views to himself!

Thinking perhaps that London doctors might be more ready

to give a new idea a hearing, Jenner paid a visit to the capital. His reception was not encouraging. He was held in high esteem as a naturalist, but this idea of cowpox inoculation did not increase his reputation as a doctor. He left London disappointed but not discouraged, and resumed his investigations on his own.

The London doctors cannot altogether be blamed. This country doctor had brought them only a theory, with little evidence apart from a legend popular among the people living in his district. He had not brought any practical proof in support of his theory—indeed, on his own admission he had never put it into practice at all.

Jenner saw that, too. John Hunter was dead, but his teaching lived after him. The countryman remembered his old master's advice: "Why think? Why not try the experiment?"

On May 14, 1796, he followed Hunter's advice.

The Crucial Test

For simplicity and clearness Jenner's own account of the experiment cannot be bettered. It was written in a letter to a friend:

> A boy named Phipps was inoculated in the arm from a pustule on the hand of a young woman who was infected by her master's cows. Having never seen the disease but in its casual way before, that is, when communicated from the cow to the hand of the milker, I was astonished at the close resemblance of the pustules in some of their stages, to the variolous [*i.e.*, smallpox] pustules. But now listen to the most delightful part of my story. The boy has since been inoculated for the smallpox which, as I ventured to predict, produced no effect. I shall now pursue my experiments with redoubled ardour.

To-day the very thought of such a dangerous experiment would be enough to make a doctor hold up his hands in horror. To inoculate anyone with the virus of smallpox would be nothing short of criminal. Jenner himself had been a bit apprehensive about the possible results of his experiment, too—otherwise he would have tried it long before. But it was not the inoculation with smallpox that worried him; that was an

everyday occurrence, a recognized preventive measure. It was the inoculation with cowpox that made him hesitate!

Jenner made two further successful experiments, and in the spring of the following year he submitted his results in the form of a paper to the Royal Society. The paper was not published. The Royal Society explained to him that it was in his own interests that it should not appear. He had made a good impression with his other papers, notably one on the life-history of the cuckoo, and it would be foolish of him to risk his reputation on this cowpox idea.

But there was no stopping the country doctor now. He continued his experiments, trying the effect of inoculations direct from the pustule on the cow's udder. The result was the same. Once cowpox had developed, smallpox could no longer be contracted.

In 1798 Jenner published his results at his own expense, in a paper entitled, "An Inquiry into the Causes and Effects of *Variolæ Vaccinæ*, a Disease discovered in some of the Western Counties of England, particularly Gloucestershire, and known by the name of Cowpox."

The paper did not have a good Press. Those who read it showed utter disbelief, and it looked as if the Royal Society had been right about Jenner's reputation. Then one London doctor was moved to try the experiment himself—and Jenner had one follower. Others came soon after, and the profession began to take sides. Vaccination, as it was called (from the Latin word *vacca*, meaning 'a cow'), had arrived. Jenner was becoming famous. His friends urged him to go to London, where he would certainly make a fortune. His reply was typical.

"Shall I," he asked, "who even in the morning of my days sought the lowly and sequestered paths of life, the valley, and not the mountain, shall I, now my evening is fast approaching, hold myself up as an object for fortune and for fame? . . . And as for fame, what is it? A gilded butt, for ever pierced with the arrows of malignancy."

Whether he wanted to go or not, however, London needed him. There were no cows in the capital, and none of the doctors

had anything like Jenners' extensive knowledge of the animals' disease. Mistakes were being made over the collection of the vaccine, and failures were reported. It took Jenner three months to get the Londoners working on the right lines.

In 1800 Jenner published his latest figures. Under his supervision 6000 people had been vaccinated, and most of them—horrible as the thought now sounds—were subsequently inoculated with smallpox. Not one had contracted the latter disease. Jenner had also made the important observation that vaccination could save people from smallpox even if given after exposure to infection.

The Spread of Vaccination

Of course there was still considerable criticism. One learned doctor propounded the theory that vaccination laid people open to all the diseases of cattle; another solemnly testified that the face of a boy who had been vaccinated was "in a state of transformation and assuming the visage of a cow." But these were exceptions, and Jenner received a good deal more acclamation than mankind generally bestows on its benefactors.

Vaccination was exported to the continent. The King of Spain fitted out a special expedition to take it to all the Spanish colonies. The Empress of Russia, with more enthusiasm than good taste, gave instructions that the first Russian child to be vaccinated should be christened 'Vaccinov.' (It must be said in her favour that she made amends to the child by conferring a State pension for life.) The Americans, who had been very unfortunate with the use of smallpox inoculation, quickly adopted the new idea, President Jefferson being among the first to be vaccinated. Vaccination was taken to the countries where it was most needed—in the East. It even reached the Red Indians of North America, who sent Jenner an eloquent testimonial that must have affected him a good deal more than the Empress of Russia's gift of a diamond ring. It ran as follows:

> Brother! Our Father has delivered to us the book you sent to instruct us how to use the discovery which the Great Spirit made

to you, whereby the smallpox, that fatal enemy of our tribe, may be driven from the earth. We have deposited your book in the hands of a man of skill whom our great Father employs to attend us when sick or wounded. We shall not fail to teach our children to speak the name of Jenner, and to thank the Great Spirit for bestowing upon him so much wisdom and so much benevolence. We send with this a belt and a string of wampum in token of our acceptance of your precious gift, and we beseech the Great Spirit to take care of you in this world and in the land of spirits.

The name of Jenner became a household word. On one occasion he was persuaded to use his influence by writing to Napoleon asking for the release of some British internees. The prisoners were released, Napoleon declaring, "Jenner!—Ah, we can refuse nothing to that man!"

But fame, Jenner had said, was "a gilded butt, for ever pierced with the arrows of malignancy." He did not want all this publicity. He wanted to be left in peace in Berkeley, looking after his ordinary patients. Surely there was never such a case of greatness being thrust on anyone. London claimed him. The societies that had once derided his theories now begged him for lectures. He was summoned to audiences with the King and Queen, and appointed physician extraordinary to His Majesty. Cities hastened to confer their freedoms on him, universities awarded him honorary degrees. Finally he was persuaded to take a practice in Mayfair. But he did not stay there for long; Berkeley was his home, and to Berkeley he returned.

Meanwhile, it had suddenly occurred to people that Jenner had made nothing out of his discovery. He had given it, freely and openly, to the whole world, asking nothing in return—except the peace and quiet the world denied him. Had he kept it a secret he could have made a fortune. As it was, he had not even got back the money he had spent on the researches of twenty-five years. Some remuneration had to be made, and in 1802 Parliament voted him the sum of £10,000. After a few years, during which the incidence of smallpox fell by leaps and bounds, Parliament decided it had been a bit mean, and a further £20,000 was awarded.

To the last Jenner remained the simple, retiring country gentleman he had always been. He ended his days in his beloved Berkeley, as the ordinary country doctor again, vaccinating the poor in his garden, and spending his leisure hours in the study of birds and animals. He died in 1823, seventy-one years old, and was buried quietly in the village churchyard.

Before Jenner

It was a 'country superstition' that had first started Jenner on his investigations; and after his discovery had been made, it was found that one 'ignorant peasant' had usurped the medical profession and actually vaccinated his wife and two sons before vaccination was discovered! The peasant was a farmer named Benjamin Jesty, and he had performed this presumptuous deed in 1774, when a smallpox epidemic was raging.

Jenner's glory was hardly diminished by this news. Jesty had apparently not repeated his experiment, nor did he bother to pass the idea round. Indeed, fifteen years later he allowed his sons to be given a standard smallpox inoculation during another epidemic. One of the young men, it is said, developed the usual mild fever, but the other had no after-effects whatever. It was quite a good tribute to Jesty's technique, but hardly enhanced his claim to fame.

The epitaph on Jesty's tombstone records that he was "an upright, honest man, particularly noted for having been the first person (known) that introduced cowpox for inoculation, and who, from his great strength of mind, made the experiment from the cow on his wife and two sons in the year 1774."

After Jenner

The results of Jenner's discovery were both immediate and far-reaching. Smallpox epidemics were controlled and finally stamped out; and a simple means was at hand to prevent them from ever recurring. An idea of the meaning of this can be gained from reference to the figures quoted at the beginning of this chapter.

Edward Jenner was not a laboratory scientist. He made a great practical discovery, and was concerned only with its acceptance and universal adoption. He did not seek reasons, but was satisfied with results. Why the inoculation of cowpox should prevent smallpox was a mystery; that it did so was a fact, and millions of lives were saved as a result. Not till more than fifty years after his death was the principle behind it revealed—the principle of immunity; and then, significantly enough, it was a knowledge of Jenner's work that played a large part in its revelation. And it was the principle of immunity more than anything else that led to the modern specialty of preventive medicine.

Jenner was one of the real heroes of medicine. He was also one of the noblest characters. He combined a love of nature with a love of humanity, and at the height of his fame his only ambition was to be with his poor villagers and his dumb friends of the woods and fields. Something of his natural simplicity and goodness of character can be seen from one of the many verses he left, entitled *Address to a Robin*:

> Come, sweetest of the feather'd throng!
> And soothe me with thy plaintive song:
> Come to my cot, devoid of fear,
> No danger shall await thee here.
> Thy cup, sweet bird, I'll daily fill
> At yonder cressy, bubbling rill;
> Thy board shall plenteously be spread
> With crumblets of the nicest bread.

This may not be great poetry, but it reveals the greatness of heart that was so characteristic of this human benefactor.

9

THE CONQUEST OF PAIN

IT is a matter of argument whether life is better to-day than it was a hundred years ago. One thing, however, is certain: it is nothing like so painful.

To-day, when the doctor advises an operation the patient does not feel exactly pleased about it. He is usually apprehensive and a bit nervous, and very glad when it is all over. But the doctor's pronouncement does not fill him with terror.

It did a hundred years ago. Then, an operation meant lying on a table fully conscious, usually tied down with strong ropes, seeing and hearing and, above all, feeling while the surgeon cut and sawed and stitched. The thought makes us shudder to-day; but then, it was an inescapable reality.

Pain has not been completely conquered, nor will it ever be. Nothing in Nature is without a purpose, and a certain amount of pain must always be regarded as a necessary evil. It tells us when we are sick or wounded, and enforces us to take rest when our bodies need it. Indeed, without any pain at all life would be extremely dangerous. We could be seriously injured without realizing it; we could die of a disease without being aware we had contracted it.

But although it is necessary that we should feel an attack of appendicitis, it is very undesirable that we should feel the appendix being removed. Again, an aching jaw may give valuable information about a decayed tooth; information of this nature is hardly welcome when the tooth is being extracted.

Is it any wonder, then, that the discovery of anæsthesia has been described as science's greatest gift to humanity?

Drugs

Man's first attempt to conquer pain was by incantations to spirits. His second, more practical method was taking drugs.

The favourite narcotics of the ancient world were mandragora, opium, Indian hemp, and hashish. The first of these was apparently the most favoured, and is believed to have been introduced to medicine by the Egyptian Sun God, Ra. The Chinese, however, were probably the first people to use narcotics in surgical operations. Much later, the Romans left precise instructions concerning the administration of mandragora, and one of Nero's army surgeons recommended its use specifically for "those who are about to be cut or cauterized." The narcotic effects of both mandragora and opium were noted by Shakespeare in the tragedy of *Othello*:

> Not poppy, nor mandragora,
> Nor all the drowsy syrups of the world,
> Shall ever medicine thee to that sweet sleep
> Which thou ow'dst yesterday.

The barber-surgeons of the Middle Ages, however, put little faith in such drugs. To be really effective, they found, the dose had to be large enough to be lethal. Many of them preferred alcohol, which was comparatively harmless, and the Italian plastic surgeon Tagliacozzi would not start on a nose-graft until his patient had drunk himself into a stupor.

Another method discovered by the Romans, which later engaged the serious attention of Ambroise Paré, was the compression of the arteries leading to the brain. By this means insensibility could easily be obtained—but the danger of death or paralysis was very great. The best surgeons of the Renaissance, therefore, had to ask their patients to grin and bear it.

Mind over Body

The sufferer from pain will try almost anything to gain relief. He has nothing to lose—except the pain. Any new idea, however unlikely, was always worth a trial. When, therefore, towards the end of the eighteenth century, a Viennese doctor told the people of France that he could banish pain with a couple of magnets, he was sure of a good hearing.

The doctor was named Franz Anton Mesmer, and from all

accounts, which are obviously highly coloured, he achieved amazing results. His method was to place his magnets on the body of the patient—that was all. Later he simplified his method still further, using only a wooden rod which, he said, he had invested with his own personal magnetism. One day he mislaid his 'magic wand'; not wishing to disappoint his patients, he touched them with his bare hands. The result was the same.

There was nothing original about this last method of Mesmer's. Medieval kings in many countries had been famed for their power to heal in just this manner, and the 'Royal Touch' had even been in vogue among the Roman Emperors. They didn't put it down to magnetism, of course; it was sufficient that they were kings.

Finally Mesmer went even further than this, and found he could banish pain and disease merely by exerting his will. That, of course, was what he had been doing all the time. Mesmerism, as it was called, was merely another name for what we now know as hypnotism.

The extent to which Mesmer's claims were justified is unknown, as reliable records are unavailable. It is certain, however, that whatever success he had was greatly exaggerated. Hypnotism is now accepted as having a rational basis, but its powers are known to be strictly limited. It has long since passed from the realm of anæsthesia to the modern science of psychiatry.

Laughing Gas

Nitrous oxide was discovered, shortly after oxygen, by Joseph Priestley. It was nearly thirty years, however, before its intoxicating effects were observed by Sir Humphry Davy. He gave it the name of 'laughing gas,' but he took it seriously enough. "As nitrous oxide in its extensive operation appears capable of destroying physical pain," he wrote, "it may possibly be used with advantage in surgical operations."

His findings were published in 1800, but a further twenty-four years were to elapse before anyone put his suggestion into

practice. Then Dr Hickman of Ludlow read Davy's work and tried nitrous oxide on dogs, mice, and other animals, with very good results. Hickman reported his experiments to the Royal Society, but that august body took him no more seriously than it had taken Edward Jenner. Most humiliating of all, the President himself showed not the slightest interest—and the President at that time was none other than Sir Humphry Davy. Hickman did not give up hope, but continued his experiments. Unfortunately his work was cut short by his death in 1830, at the age of twenty-nine.

Meanwhile laughing gas had found its way to America, and it was soon living up to its name. Young Americans, seeking novelty, had found a way of getting drunk without drinking, and parties were held for the sole purpose of inhaling this remarkable gas. One such party was attended by a young dentist named Horace Wells, who made the significant observation that in their exhilaration the revellers could hurt themselves without noticing it. Wells was interested—so interested that he decided to sacrifice a perfectly good tooth of his own to find out more about it. At his request a colleague removed the tooth while Wells was under the influence of nitrous oxide. He felt nothing. "A new era in tooth-pulling!" he exclaimed, when he came round.

That was in 1844, and early in the following year Wells gave a demonstration to the professors and students of Harvard University. Too late he realized that he should have bided his time. He did not know enough about the gas, and administered an insufficient dose. The patient let out a yell of pain; the audience, sceptical to begin with, gave Wells no second chance.

Still he did not learn his lesson. Ambitious and impatient, he hurried to give another public demonstration, this time in his home town. The result was tragic. Determined not to repeat his mistake, he made the dose too large, and the patient died. Wells was unnerved by this. He lost his confidence and finally had to give up dentistry altogether. He never recovered from the blow; and three years later this promising young man lost his reason and committed suicide.

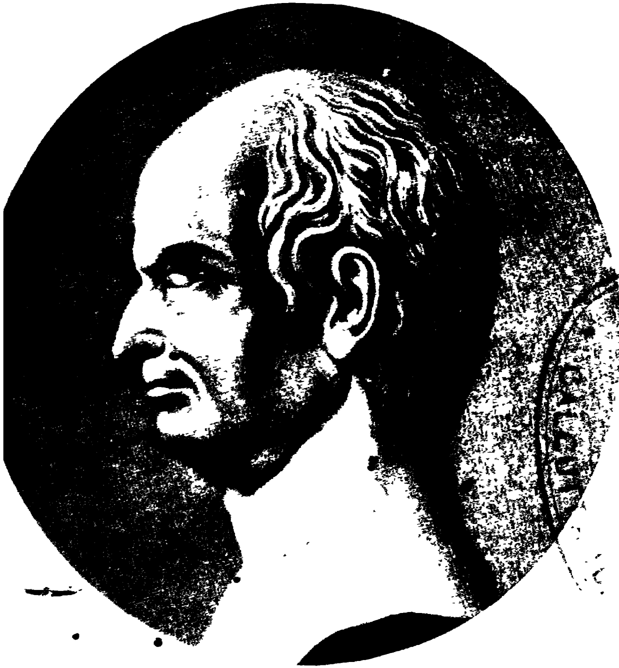
Sulphuric Ether

Horace Wells had a partner. His name was William Morton, he was a few years the junior, and he had assisted in the ill-fated Harvard demonstration. After this and Wells's second disastrous experiment Morton felt little inclination to make further trials with nitrous oxide. Laughing gas was no joke. Nor, however, was cold-blooded tooth-pulling, and Morton by no means despaired of finding another way to overcome pain. In 1846 Dr Charles Jackson of Harvard drew his attention to a chemical known as sulphuric ether.

Ether had been discovered in 1818 by Davy's famous assistant, Michael Faraday. It gained much the same notoriety in the United States as nitrous oxide, and 'ether frolics' were soon the rage. Dr Jackson now suggested its use in dentistry, and Morton needed no second bidding. Obtaining a supply of the precious drug, he locked himself in his surgery and tried it out. Within a short time he lost consciousness, and when he came round again he knew he had found what he needed. Without hesitation he tried it on his next patient, with unqualified success. He began to use it regularly; the news spread; painless dentistry had arrived.

But Morton was something more than a dentist. He had foresight and imagination, and already he was considering the practical application of the drug to general surgery. For that, he knew, the period of unconsciousness would have to be longer than what he had so far obtained; and he began to experiment on himself again, taking steadily increasing doses. He knew he was risking his life, but he was determined to be more patient than his unfortunate partner. Not until he was convinced of the efficacy of the drug did he seek to give a practical demonstration.

Dr Warren, senior surgeon of Massachusetts General Hospital, gave the young dentist his opportunity. On October 16, 1846, in the presence of a crowd of doctors and students, the first surgical operation under anæsthesia was performed. Morton was late—so late that Dr Warren, tired of waiting, had actually picked up his knife in readiness to begin without him. Then



PASTEUR'S PREDECESSOR: THE ABBÉ SPALLANZANI

PASTEUR'S PUPIL: ILYA METCHNIKOFF

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A CHEMICAL LABORATORY IN THE EIGHTEENTH CENTURY

Morton arrived, full of apologies, which the surgeon brushed aside.

"Well, sir," he told the twenty-seven-year-old dentist, "your patient is ready."

Morton bent over the patient and applied the inhaler to his mouth. A few minutes later he straightened up and faced the surgeon.

"Sir," he said, "*your* patient is ready."

The operation was for a tumour on the neck. The surgeon worked quickly and methodically, all his attention on the job in hand. The patient did not move or utter a sound. The wound was sutured and dressed. The patient began to come round. Dr Warren faced the assembled spectators and said:

"Gentlemen, this is no humbug!"

The Ether Controversy

The sequel to this wonderful event forms the most sordid and most distasteful story in medical history. U.S. Congress, with more enthusiasm than wisdom, decided to show a practical appreciation of this great boon to humanity. Accordingly the sum of 100,000 dollars was formally voted for the discoverer of anæsthesia. It only remained for him to come forward. . . .

They all came forward. Not only Morton and Jackson, but the relatives of the late Horace Wells, too. Congress set up a Committee to consider the rival claims. At first it looked like a straight fight between Morton and Jackson; and the poet Oliver Wendell Holmes, who gave anæsthesia its name, suggested the erection of a memorial with the statues of both, inscribed, "To E(i)ther."

Then came a bombshell. Ether had been used as an anæsthetic four years before Warren's operation—by a country doctor named Crawford Long. He too had first met the drug at a 'party,' and he had investigated its properties entirely on his own account. He had used it in his surgery for eight minor operations, all successful, the first being performed in 1842. Certainly he had not dreamed of its wonderful possibilities; and the disapproval of almost the whole of his practice had eventually

led him to abandon it. But he had been the first; he could even produce a receipted bill to prove his point—a bill for two dollars for the operation and twenty-five cents for the ether!

This was more than Congress had bargained for. But worse was to follow. As if by magic, three more claimants appeared. Apparently ether had been in use all over the States before Jackson and Morton had heard of it. Then the relatives of the late Dr Hickman wrote from Ludlow and suggested that if the matter could not be settled in America, the money could well be used in England, where anæsthesia was really born.

The matter was thrashed out in public and in private. The claims were examined and re-examined. For eight long years the controversy raged. Then, at last, the Committee made its final report: a decision could not be reached.

The award was never made.

The Discovery of Chloroform

Two months after Warren's historic operation sulphuric ether was tried as an anæsthetic in the land of its origin. London's most famous surgeon, Robert Liston, performed the operation at the University College Hospital. "Gentlemen, we are now going to try a Yankee dodge for making men insensible," he announced. It was a case of amputation of the leg. It took Liston precisely twenty-six seconds to remove the limb. To ears long accustomed to terrible cries of agony the silence was uncanny. Then the patient came to his senses. "When are you going to begin?" he asked.

"In six months no operation will be performed without this previous preparation," prophesied the surgeon.

Within twelve months another preparation had threatened to supersede it entirely.

The story of chloroform is the story of James Young Simpson, seventh son of a village baker. Born in 1811, he was enabled, by the sacrifices of his parents, to study medicine at Edinburgh University. So successful did he become that by the time the anæsthetic was first introduced Simpson was worth over £4000 a year. Yet he had very nearly renounced medicine while still

a student. This was after he had seen a surgical operation for the first time. The agony of the patient made a terrible impression on the youth; if he could not do anything about it, he decided, it would be better not to practise medicine at all. But perhaps—perhaps he might be able to do something about it. . . .

Simpson deliberately specialized in the painful practice of midwifery. His work quickly attracted attention, and when only twenty-eight years old he was appointed professor at Edinburgh University. Meanwhile, he had already started his long search for something to alleviate the suffering that he witnessed daily. He even gave mesmerism a trial.

Then came the dramatic news of Liston's operation. Simpson hastened to London to find out all about the anæsthetic, and three weeks later he was back in Edinburgh trying it out. The efficacy of the drug was undeniable. In spite of his enthusiasm, however, Simpson saw it only as a beginning. Sulphuric ether was difficult to administer, its odour was unpleasant and persistent, the after-effects were bad. The principle seemed perfect; it was only the agent employed that did not satisfy him.

Simpson went to the chemists. If there was anything better than sulphuric ether he was going to find it. With two colleagues, Doctors Duncan and Keith, he started on a series of investigations on every drug that might conceivably serve the purpose. His drawing-room became a gas-chamber, and night after night the trio sat together, inhaling various preparations. Like Morton, Simpson was fearless to the point of folly. On one occasion he was saved from certain death only by the insistence of a chemist that a certain new drug should first be tried on a rabbit. The rabbit died, and Simpson lived to carry on. Another time, when he was experimenting by himself, he lay unconscious for two hours.

The search went on for nearly a year. Then one of Simpson's chemist friends suggested chloroform. Simpson was not very hopeful, but he took a sample home with him. He had guests that evening, but the experiments went on as usual. The new drug was found to be delightfully heady, and the party soon

began to get quite hilarious. Then there was a crash: the professor had fallen to the floor. The next part of the story has been graphically described by another colleague of Simpson's, Professor Miller:

> On awakening, Dr Simpson's first perception was mental: "This is far stronger and better than ether," said he to himself. His second was to note that he was prostrate on the floor, and that among the friends about him there was both confusion and alarm. Hearing a noise, he turned round and saw Dr Duncan beneath a chair—his jaw dropped, his eyes staring, his head bent half under him, quite unconscious and snoring in a most determined and alarming manner. More noise still—much motion. And then his eyes overtook Dr Keith's feet and legs making valorous attempts to overturn the supper table, or, more probably, to annihilate everything that was on it.

Experiments were carried on till the early hours of the morning, and one of the ladies, who was permitted to take an active part, amused every one by crying, "I'm an angel! Oh, I'm an angel!"—and then falling into a deep sleep.

The first patient on whom Simpson used chloroform was the wife of another doctor. The result was entirely successful, and the child born—a girl—had the doubtful pleasure of spending the rest of her life answering to the name of 'Anæsthesia.' Shortly afterwards Simpson gave his first public demonstration of the new anæsthetic. Three major operations were performed in succession, before a crowd of doctors and students. In every respect chloroform was acknowledged to be better than sulphuric ether.

A fierce controversy followed Simpson's discovery, but of a very different nature from the American wrangling. This time it was a question of morals. Chloroform had been introduced for the specific purpose of alleviating the pains of childbirth; and a number of eminent men gave it as their opinion that it was unnatural and evil to use artificial agents to deprive women of the privilege of this traditional agony. (What the wives of these eminent men thought was, apparently, nobody's business.) The Bible was quoted in support of the contention, especially

the passage in Genesis reading, "In sorrow thou shalt bring forth children." Simpson was undismayed. The Devil, said Shakespeare, could cite the Scriptures for his purpose. The professor gave as good as he got by pointing to another passage in Genesis, which he claimed to be a record of the very first use of anæsthesia—"And the Lord God caused a deep sleep to fall upon Adam, and he slept; and he took one of his ribs, and closed up the flesh instead thereof."

The argument went on for eight years. Then Queen Victoria settled the matter by having chloroform administered to her during confinement. After that there was nothing more to be said. Queen Victoria's morals were above reproach. Simpson was created a baronet, and chloroform had come to stay.

Simpson was one of the greatest of all Scots, and he has not been forgotten in the land of his birth. When a new midwifery department was recently added to the Edinburgh Royal Infirmary it was appropriately given the name of the Simpson Memorial Wing.

Later Developments

Shortly after chloroform was introduced it seemed as if it would replace ether altogether. Later, however, the old sulphuric ether gave way to a purer drug, and at the same time improvements were made in the technique of administration. Ether came back into favour, and it has held pride of place ever since—although chloroform is still preferred in one part of the world: Scotland, where it was first used.

Laughing gas, too, had a revival towards the end of the nineteenth century, and it was firmly re-established for the very purpose for which it had first been introduced—the extraction of teeth.

It was inevitable that doctors should seek other methods of administering anæsthetics apart from the inhalations through the mouth and nose. In certain facial operations, indeed, a different technique was practically essential. Claude Bernard, whose story is reserved for a later chapter, suggested the use of the hypodermic syringe for the purpose; and chemistry,

medicine's indispensable supply depot, provided the materials. One of the latest drugs to be used in this way is pentothal sodium, which is administered by injection into the veins, producing full surgical anæsthesia just like ether and chloroform. Because of its simplicity of administration it was used extensively in the battle-zones in the 1939–45 War. Complete insensibility can thus be produced by the prick of a needle, and the present-day anæsthetist has at his disposal a fine array of drugs and a variety of means of administration.

With the notable exception of the work of Simpson, the history of anæsthesia belongs almost entirely to the United States. Thus it is America that we must thank for what is known as 'local' anæsthesia. This is, of course, simply sending to sleep the particular part of the body where pain is expected to occur. It is generally administered by the hypodermic syringe, and the first agent used was cocaine.

Cocaine was discovered in Vienna in 1884, by Carl Koller. Koller could not take the whole credit, however, as he merely completed the work which a friend of his had left off. The latter probably would have himself succeeded had he valued his researches more highly than seeing his fiancée. Perhaps he may be excused, however, as anæsthesia was hardly his province; for the name of the delinquent was Sigmund Freud, founder of psycho-analysis.

Cocaine was first injected under the skin, but within a year of its discovery far-reaching improvements in technique had been made. The American surgeon W. S. Halstead was the first to inject it into the nerves, and almost immediately afterwards J. L. Corning, another American, introduced the famous 'spinal' anæsthesia. This consisted of an injection into the sheath of the spine, thereby producing insensibility in the entire lower part of the body. This method was rendered almost perfect by the discovery in 1909 of the famous drug known as stovaine, which eventually superseded cocaine altogether. The wonder of spinal anæsthesia needs to be seen to be believed. By the employment of this method a man can read a book and smoke a cigarette while his abdomen is cut

open or his leg amputated. Indeed, when spinal anæsthesia was first introduced surgeons had quite a race for the honour of being the first man to remove his own appendix—and one of them even assisted in the amputation of his leg!

Only one thing modern anæsthesia has not yet succeeded in doing: that is the elimination of what is called 'surgical shock.' Pain may be eliminated, but the body is not deceived; and shock is the commonest cause of death in injuries. It is the reduction of surgical shock that is the main goal of present-day anæsthetic research.

10

THE MICROBE REVEALED

THE story of the microbe is the story of the microscope. Not only did its discovery depend entirely on the use of this instrument; but the invention of the microscope made that discovery practically inevitable.

The Microscope

Very little, unfortunately, is known of the history of the microscope. Its invention has been ascribed by some authorities to the Greeks, but the evidence suggests that they made little practical use of whatever form of the instrument they had. It was not until the beginning of the seventeenth century that the principle of the double lens was discovered by a Dutch spectacle-maker named Jansen, and introduced in the telescope and microscope by Galileo. Galileo, as is well known, spent much of his life looking through the larger of these two instruments; the compound microscope, however, did not come into general use for another two centuries.

Meanwhile the simple lens was greatly improved, and it was through this instrument that Malpighi saw the capillaries that had evaded William Harvey's patient research. Malpighi made a number of other useful observations, and a contemporary of his, Athanasius Kircher, was the first to see the red corpuscles of the blood, although he did not recognize their true nature. The man who discovered the microbe, however, was not a professional scientist at all, but a prosperous Dutch merchant whose first experiments were in the nature of a hobby. His name was Antony van Leewenhoek, and his hobby soon developed into a life-interest. He made his microscopes himself, and his early work was mainly an elaboration of the discoveries of Malpighi and Kircher. Then, in 1683, he made one of the most important discoveries in the history of medical

science: examining the tartar from his own teeth, he found what he termed "very small animalcules, the motions of which were very pleasing to behold." (Had he known the capabilities of these little creatures Leewenhoek might have been less charmed by their appearance!)

In the nineteenth century Galileo's compound microscope became an instrument of practical value, and the old simple lens was discarded. Results quickly followed. Rudolf Virchow revolutionized the science of pathology with his discovery that Hippocrates was wrong for once, and the human body was not, after all, made up of four 'humours,' but consisted of a vast number of what he termed 'cells.' He showed that cells multiply, and that every existing cell came in its turn from another cell—"*omnis cellula e cellula*."

At almost exactly the same time as Virchow was destroying a cherished belief of twenty-two centuries, the new compound microscope was being used in the greatest discovery in the whole history of medicine. The discoverer was not a doctor, but a chemist; yet in his lifetime he succeeded in changing the very fundamentals of both medicine and surgery, and his name is unchallenged in medical history.

That name, of course, is

Louis Pasteur

Louis Pasteur was born in 1822 in the French town of Dôle. His father was a tanner, his mother the daughter of a market-gardener. As a schoolboy Louis showed a taste for art rather than science, and it was not until he was seventeen that chemistry began to interest him. His parents made every sacrifice to give him a good education, and eventually he gained admission to the École Normale in Paris. He graduated in chemistry and physics, got a job in a Paris laboratory, and started some research-work on his own account.

His first investigations were concerned with the study of crystals, and within four years he was reading papers on the subject to the Academy of Science. Now a Doctor of Science, he was appointed successively to the Chair of Physics at Dijon

and of Chemistry at Strasbourg. He retained the latter post until 1854, when he became Professor of the Faculty of Science at Lille.

Lille was a large industrial town; one of its industries was the manufacture of alcohol from beetroot; and the father of one of Pasteur's pupils was engaged in this trade. Professor Pasteur was an accessible man. The manufacturer contacted him through his son and acquainted him with some of the problems of his trade. His products had a habit of turning out badly; he could find no reason for this; could the Professor suggest anything?

Thus it was that Louis Pasteur began his studies on fermentation.

The Mystery of Fermentation

The nature of fermentation had been the subject of a bitter controversy only twenty years previously. This was now history, however, the question having been—as was thought—finally settled. It was another Frenchman, Cagniard Latour, who started it all by ascribing the fermentation of beer to what he termed 'budding' of the yeast. A German chemist, Schwann, came to the same conclusion independently, and suggested that fermentation was a vital process. At this juncture, however, the great chemist Liebig intervened. With withering scorn he compared such a belief with "that of a child, who would explain the rapidity of the Rhine current by attributing it to the violent movement of the many mill-wheels at Mainz." Liebig seemed to settle the matter by defining fermentation as a purely chemical change, and only a bold man would have dared to question such an authority.

But then Pasteur was a bold man.

He began by repeating the experiments of Latour and Schwann. He observed the 'budding' of yeast, and was convinced that the change of sugar into alcohol could be no mere chemical process, but was the direct result of *vital* activity on the part of the yeast-cells. Pasteur then turned his attention to two other forms of fermentation—the processes whereby milk turns sour and butter rancid. He quickly recognized that

once again living organisms were at work—but this time of a different kind. By experiment he showed that each form of fermentation was caused by a specific organism, and that these organisms were not only alive but continually reproducing themselves. When milk sours little grey streaks appear; by 'sowing' these in tiny quantities into fresh boiled milk Pasteur was able to produce fermentation at will.

In the middle of these researches Pasteur left Lille to return to the École Normale in Paris—this time as a Professor of Science. His request for a laboratory was refused, and it was in the corner of a loft that he made the discoveries that were soon to be revealed to a sceptical world.

No longer was he concerned merely with the process of fermentation. He was working on a far bigger subject—on the very subject of life itself. Fermentation was caused by living organisms; where, he asked, did these organisms come from? "This is the problem," he told the Academy of Science, "which has led me to the study of spontaneous generation."

Spontaneous Generation

One of the problems which the Greeks thought they had solved was the cause of what is known as putrefaction, or decay. When meat goes bad, maggots appear, and this was regarded as a typical example of the phenomenon of 'spontaneous generation.' The principle behind this theory was simply that living beings could, in certain conditions, be spontaneously produced by dead matter. Aristotle affirmed that frogs and eels were 'generated' daily in this manner; and the Latin poet Virgil even went so far as to give a prescription for 'creating' bees:

> Kill an ox two years of age, whose young horns are just beginning to curl on his brow, place him in a narrow enclosure strewed with freshly gathered leaves of thyme and rosemary, and soon from his fermenting humours there rises a swarm, which fills the air like rain from summer clouds.

As the whole question of the origin of life was (as it still is) shrouded with mystery, there was nothing unreasonable in this

belief. It persisted until the Renaissance, when the new spirit of scientific inquiry caused it to lose ground. Ironically enough, the discovery of microbes served to revive it—although Leewenhoek himself indignantly denied that his "animalcules" could be produced in any such manner. "Surely no one will be so absurd," he wrote, "as to retain the notion that any animal, however contemptible in our eyes, can be produced spontaneously or bred from corruption."

Many eminent scientists were just so absurd, but they can hardly be said to have merited this criticism. Leewenhoek himself failed to offer any alternative explanation for the source of his animalcules. Nor did Francesco Redi, the Italian poet and naturalist; but by a simple experiment he gave a very convincing proof against the theory. He covered a piece of meat so that the flies could not reach it—and no maggots appeared on the meat. This experiment, which took place in 1684, did not make a great impression on the world of science, for in the next century a Catholic priest, Father Needham, reasserted the theory of spontaneous generation in a most dogmatic fashion. His experiment consisted of putting some putrescible liquid in an air-tight vessel and heating it, to kill off any living organisms that might already be there. He left the vessel sealed, and a few days later he was able to point to putrefaction setting in as usual. He therefore challenged anyone to deny the truth of spontaneous generation.

The challenge was taken up by an Italian, Abbé Spallanzani. He proved the exact opposite simply by copying Needham's experiment but applying a little more heat. Undismayed, Needham retorted that Spallanzani had used so much heat that he had corrupted the "vegetative force" of his infusion and polluted the air. To this, unfortunately, the Italian could offer no effective counter-argument, and there the matter rested.

The Germs We Breathe

That there were living organisms in the atmosphere had been suggested more than once, and it was to the contents of the air

around him that Louis Pasteur turned his attention. He drew air through a wad of cotton wool, and examined the dust that was collected. The microscope revealed that it was teeming with organisms.

Next, Pasteur repeated Spallanzani's experiment—but with a difference. He heated a putrescible solution, then sealed the flask, and left it long enough to show that putrefaction could not occur. Reopening the flask, he dropped a minute part of his dirty cotton wool on to the pure fluid—and putrefaction quickly set in. Father Needham's "vegetative force" had not been destroyed, after all.

Such was the simple experiment which led to the final disproof of the theory of spontaneous generation, and the inception of the germ theory of disease. Spontaneous generation, declared Pasteur, was a chimera. Putrefaction was simply a fermentation caused by the presence of living organisms which came from the air—microbes.

Needham's disciples were not so easily satisfied. Fresh "vegetative force" could have been supplied by the cotton wool, they said. Furthermore, there remained the charge of 'pollution' of the air in the heated flask.

These were quite legitimate objections, which could only be refuted by a demonstration that allowed the air free access to the putrescible liquid all the time. The problem was, therefore, to find a means of letting in the air but keeping out the invisible microbes that lived in it. Pasteur's solution was again brilliant in its simplicity. Heating the liquid but leaving the flask unsealed, he bent the neck into an S-bend. The flask was then left in a closed room, and subsequent examination, even months later, revealed no sign of putrefaction. The microbes were in the air, of course, and it was no fault of theirs that they failed to reach the putrescible liquid. It was on the inexorable law of gravity that the apparatus was based. Dust settles; and the microbes got no farther than the bottom of the neck of the flask. Finally, to clinch his argument, Pasteur had only to shake the apparatus to allow the fluid to run along the neck and back again—and putrefaction started.

Pasteur reported his findings to the Academy of Science in Paris, and the inevitable criticism followed. The numerous supporters of the theory of spontaneous generation raised every objection they could think of. Chief of these was against Pasteur's contention that the microbes came from the air. If this was so, one of his principal opponents, M. Pouchet, observed sarcastically, they must form a fog "as dense as iron."

Pasteur therefore decided to investigate the actual microbe-content of the air. He had long suspected that this must vary according to the amount of dust in the atmosphere, and he took his capsules, or little flasks, down into his cellar and then out into the courtyard. The results were illuminating. Exposure of ten capsules to the comparatively dust-free cellar air resulted in putrefaction in only one; in the open courtyard he exposed eleven capsules—and putrefaction followed in every one. This encouraged him to seek purer atmosphere, and he went up into the mountains. His travels ended on the Mer de Glace itself, where he opened twenty capsules, of which only one subsequently showed signs of putrefaction.

Pouchet soon had an answer to this. He and two colleagues found a mountain in Italy 1000 metres higher than the Mer de Glace, and there they opened eight capsules—and in all cases putrefaction resulted. Pasteur, however, was undismayed; microbes were to be found on one's hands and clothes as well as in the air, and it was only to be expected that men who did not believe in his theory would fail to take even elementary precautions through sheer ignorance. Meanwhile, the directors of the Academy of Science, tiring of hearing the rival claims of individual experimenters, resolved to settle the question in an entirely practical manner. They set up a committee before which Pasteur and Pouchet were invited to demonstrate at the same time. Pasteur could not have wished for a better opportunity, and his demonstrations before the committee could not be disputed. Thus his theory of putrefaction came to be accepted as true, although several years were to pass before the ghost of spontaneous generation was finally laid.

This was in 1863, and in the same year Pasteur published

his *Récherches sur la Putréfaction*, which was to revolutionize the whole practice of medicine and surgery. Pasteur had already foreseen some of the results of his discoveries. While still engaged in his controversy with Pouchet he had given a clear indication of his ambitions. "It is very desirable," he had written, "to carry these researches sufficiently far to prepare the way for a serious inquiry into the origin of disease."

The study of disease was not Pasteur's job. He was a chemist, and disease was the province of the medical profession, of which he was not a member. With few exceptions, the medical profession in France did not hesitate to tell him so.

This did not deter Louis Pasteur. In the succeeding years he devoted himself to the study of diseases of silk-worms, wine and beer, sheep and cattle, poultry, and, finally, human beings. As a result of this work he was led to advance the general 'germ theory of disease,' in which he ascribed the cause of infection to the activity of microbes. By the time this theory was announced, however, it had already been applied in practice. From the Frenchman's work on putrefaction sprang the idea of the antiseptic method, the story of which is told in the next chapter.

Silk-worms, Beer, and Cattle

In 1865 Pasteur received an urgent S O S to go to the south of France. A great industry was threatened with utter ruin; a mysterious disease was ravaging silk-worms, and the farmers were powerless against it.

Pasteur had never touched a silk-worm. He knew nothing whatever about the industry. Furthermore, he was anxious to pursue his researches on putrefaction. Yet he responded to the call. The story of his five years of painstaking toil belongs to the Romance of Agriculture rather than the present subject; suffice it to say that his mission was entirely successful. He discovered two separate diseases of the silk-worms, worked out a detailed method for their prevention, and saved the industry.

This work was by no means a waste of time from the point of

view of Pasteur's own studies. He learned a lot from silk-worms. He gained his first experience of the principle of individual susceptibility to disease, and also of the influence on this of heredity; and he learned that a microbe normally gains in virulence each time it passes through a living organism. Both these discoveries were to prove of great importance to the new science of bacteriology.

Meanwhile, at the end of 1868 Pasteur had been appointed Professor of Chemistry at the Sorbonne University—this time with the promise of a laboratory for himself. But in the same year he sustained a cerebral hæmorrhage, and for a time his life was in the balance. Fortunately he recovered, and in the following year he completed his work on silk-worms. In 1870 he paid a visit to Munich to see Liebig, whose theories he had so effectively destroyed. The meeting between the two chemists was amicable; a few days later their respective countries were at war.

Pasteur had returned to the study of fermentation, and in 1871 he visited some English breweries and explained why beer went bad and how this could be prevented. (It may be added that if there was one drink Pasteur did not like it was beer.) Back in Paris, he continued to study and teach, and in 1873 he was elected a Member of the Academy of Medicine—an unheard-of honour for a man without a medical degree. His health, however, had never been the same since his illness, and in 1874 he had to resign from his Chair at the Sorbonne. The French Parliament commemorated his services by the award of a pension for life.

But Pasteur had not the slightest intention of retiring from his work. He was only fifty-two years of age, and he felt he could give further useful service to the cause of science. In 1877 an epidemic of anthrax broke out among the sheep and cattle. The veterinary surgeons could do nothing to control it, and Pasteur was called in. For two years he laboured on the problem, which led him to investigate as well the disease of poultry known as chicken-cholera; and it was then that he made one of his greatest discoveries of all.

ROBERT KOCH'S LABORATORY IN BERLIN

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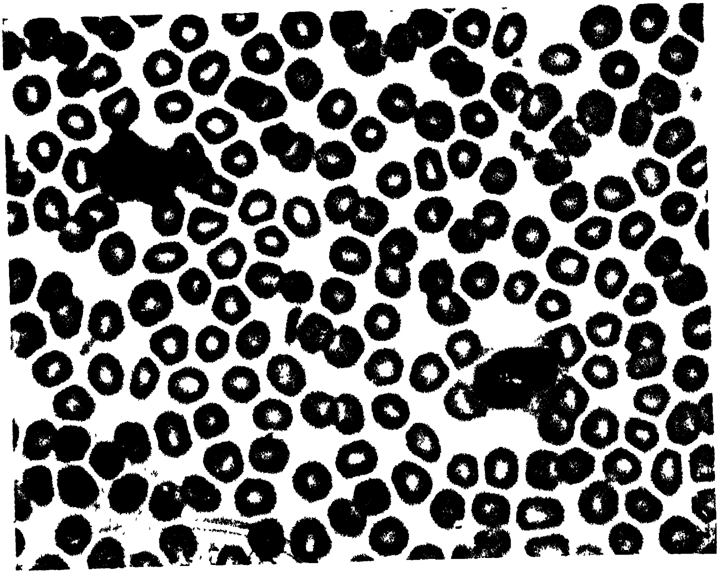
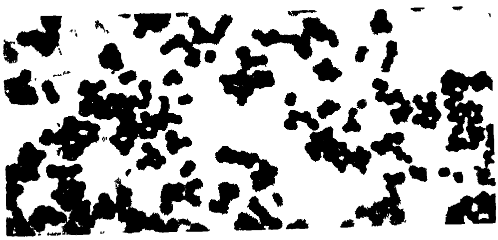


CELLS OF HUMAN BLOOD

The cells are highly magnified. All are red cells except two, which are white cells and differ by being larger and having definite nuclei.



ONE OF MAN'S OLDEST ENEMIES

STAPHYLOCOCCUS

The Principle of Immunity

In 1879, after working on a series of cultures of the microbe of chicken-cholera, Pasteur took a well-earned holiday. On his return to work he was disappointed to find that his cultures had stopped reproducing. He tried them on some fowls, which were only slightly affected; and it looked as if he would have to take fresh cultures to resume his researches. However, the fact that the fowls had been affected at all aroused his interest. He therefore took a fresh culture, and inoculated first these fowls, and then some others that had had no previous injections. The new birds contracted chicken-cholera and died; the others were unaffected.

Edward Jenner had discovered vaccination by the simple process of trying it. Louis Pasteur had discovered the principle behind all protective vaccination and inoculation by scientific research and experiment.

This principle is known as immunity, a word which comes from the Latin, its original meaning being 'exemption from military service.' Immunity in its medical sense is brought about by the presence in the blood of what are known as antibodies. Some people are naturally immune from certain diseases, having inherited those particular antibodies from their parents. Others, again, acquire antibodies in the course of an attack of a particular disease, and are thus immune from catching it again. This explains why it is unusual for anyone to contract an infectious disease, such as typhoid fever, more than once.

It has been seen how people once sought to gain immunity from smallpox by deliberately contracting a mild form of the disease; and how Jenner, who knew nothing about antibodies, actually achieved this immunization by inoculation with the virus of cowpox. The significance of Pasteur's new discovery, therefore, was that a way was now open for immunity against a specific disease to be acquired by simple inoculation from an attenuated culture of the same disease. Jenner's method could not be extended beyond the single disease which it was designed

to prevent; Pasteur's discovery, on the other hand, formed the foundation on which all subsequent protective inoculation was to be based.

Jenner's contribution must not be undervalued on this account. His achievement was all the greater because he lived before the age of modern scientific medicine. And it was the knowledge of his discovery that prompted Pasteur to try his experiment on the chickens. The Frenchman himself recognized the worth of Jenner's work, and he paid a graceful tribute to the memory of the country doctor by giving to this method of immunization the general name of 'vaccination'—which was quite incorrect, really, because it has nothing to do with cows!

Pasteur at once set to work to discover the reason why his culture had so fortunately become attenuated. It had decreased in virulence as it grew older—that much was clear; and he soon discovered that it was the influence of oxygen in the air that was responsible. This meant that he was now able to reduce the virulence of a culture to the precise degree that he required. He applied the principle to the disease of anthrax, and the epidemic was checked and finally stamped out.

As with his discoveries regarding germs, Pasteur had to leave the particular applications of his principle to other workers. They were not lacking; vaccines have been prepared against numerous infectious diseases, including typhoid and typhus fevers, diphtheria, yellow fever, cholera, plague, and, more recently, influenza. An idea of the value of vaccines may be gathered from a comparison of the typhoid fever statistics among British troops in the Boer War and the War of 1914–18, when general inoculation was first introduced. The average strength of the Army in the Boer War was little over two hundred thousand; in the War of 1914–18 it was over two million. During the former War there were 57,684 cases of typhoid, of which 8022 proved fatal; in the latter, only 20,139 cases were recorded, the mortality being down to 1191. These figures were reduced even further in the War of 1939–45.

It has just been said that Pasteur had to leave the preparation of specific vaccines to other scientists. To this there was one

important exception. At the age of sixty-three Louis Pasteur achieved his crowning success: the prevention of the dread disease of hydrophobia, or rabies.

Mad Dogs

The common cause of rabies is the bite of a mad dog. One of the most horrible features of the disease is the uncertainty of the length of the incubation period—that is, the period of time between the bite and the appearance of the symptoms. This generally lasts between two and twelve weeks—but it may be shorter or longer. During this time the person bitten may feel perfectly well, and one can only imagine the agony of suspense endured. Once the symptoms develop, however, there is nothing uncertain about the course of the disease.

The first symptoms are depression and irritability. The disease attacks the nervous system, and symptoms of mania and paralysis may soon appear. Convulsions overtake the patient, finally leading to coma and death. The sufferer is conscious to the end, and unfortunately no treatment is of any use once the symptoms have appeared.

To this day there is no record of a single case having survived.

In seeking to prevent rabies, of all diseases, Pasteur could not have chosen a more difficult task. Even if he succeeded in preparing an effective vaccine, he knew that it would never be generally adopted like Jenner's original vaccine against small-pox. The number of people bitten who contracted the disease formed a tiny percentage of the population of any district; and the risk of being bitten by a mad dog was less than that of being run over in the street, even in those days. It would have been folly to expect people to submit to such a vaccination on the off-chance of being bitten some time. A vaccine could only be useful, therefore, if it proved effective when given *after* the person had been bitten.

Pasteur began his new studies in 1880, and soon found that the work called for more than mere patience and energy. Great personal courage was required from himself and his assistants. For the collection of specimens the latter would

hold down a rabid dog while Pasteur himself put one end of a glass tube between his lips and the other between the jaws of the animal, and calmly sucked up the deadly saliva.

The responsible microbe was eventually isolated in the nervous system of an infected dog. Now Pasteur could begin in earnest on the work of preparing a vaccine. Clearly it was going to be no ordinary vaccine. The fact that it would be injected only after the dog-bite meant that the original virus would always have a start in the race; if it was to be effective, therefore, the incubation period of the vaccine virus must be correspondingly reduced.

Pasteur knew only one way by which he might achieve this reduction, and that was by increasing the virulence. After much experiment he finally accomplished this by passing the virus through ninety rabbits. The incubation period was reduced to seven days—but at the inevitable expense of a considerable increase in virulence. A single dose of such a vaccine was far more potent than any bite from a mad dog.

But Pasteur was working to a plan. To give such a vaccine by itself was out of the question; but might it not be safely received if the body were first *prepared* for it? His idea was a progressive course of vaccines, each one slightly more virulent than the last, until finally the deadly seven-day virus could be received in safety. By this means full immunity could yet be gained within the prescribed period.

The next problem was to reduce the virulence which he had so successfully increased. Pasteur's first attempt at this met with only qualified success. By transmitting his powerful virus through a succession of monkeys he was able to reduce it to a state in which it could no longer produce rabies; but to this method there were a number of practical objections, chief of which was that it called for an almost unlimited supply of monkeys! Pasteur reverted to the use of oxygen, and eventually he hit upon the idea of drying the spinal cords of the infected rabbits. Each day he noted a fresh decrease in virulence, until after exactly a fortnight safety-point was reached.

Fourteen injections, therefore, were needed. Immunity was

to be built up gradually, so that by the time the incubation period of the dog-bite virus was reached the body was fully protected against the disease. The only condition for the success of the vaccines would be how soon after exposure to infection the course was begun. That was the theory of it, anyway. Practical confirmation was another matter.

Pasteur tried it on the dog. It worked. He tried it on fifty dogs. It worked. He prepared fresh series of vaccines—and hesitated. He had devoted nearly five years to this study, and his work was ready for the final test: on a human being.

This was the end towards which Pasteur had been striving. Yet—he hesitated. It was an experiment that few scientists would care to make. However sure he might feel, no amount of trial on animals could prove that the effects on a human subject would be the same. Furthermore, the test would have to be made on some one who had been bitten by a dog that might or might not be rabid; the final vaccines in the course were of themselves more powerful than the normal virus; if the patient died, therefore, Pasteur would never know if it had not been his own vaccines alone that were responsible.

There was another way, however. "I have not yet dared to treat human beings after bites from mad dogs," he wrote; "but the time is not far off, and I am inclined to begin with myself—inoculating myself with rabies and then arresting the consequences!"

Before he could carry out this courageous proposal Pasteur was suddenly faced with the greatest crisis of his life. An unexpected visitor appeared at his laboratory. His name was Joseph Meister; he had come from Alsace; he was nine years of age; and he had been bitten two days previously by a dog which, from all accounts, was certainly mad.

With the boy were his mother and the owner of the dog. Pasteur closely questioned the latter about the animal, which he had fortunately managed to kill. The account of its behaviour and appearance left the scientist in little doubt. The boy had no fewer than fourteen wounds. Rabies seemed almost inevitable. Pasteur delayed only a matter of hours, in which he consulted

his colleagues. But the decision and responsibility were his; and on the same evening he administered the first injection.

The die was cast. As day followed day the vaccines given were steadily more virulent. Something of Pasteur's state of mind during this critical period can be seen from a letter his wife wrote to their children at the time. "Your father has had another bad night; he is dreading the last inoculation on the child; and yet there is no drawing back now."

Joseph Meister lived. Three months later Pasteur declared himself satisfied—and almost immediately another boy was brought to his laboratory. This time six days had elapsed since the bite, and an autopsy on the dog had proved it was rabid. The boy's life was saved; Pasteur had triumphed again.

The news spread, and for the next six months Pasteur had little time for any work apart from the preparation and administration of his vaccines. The statistics covering this period were truly amazing. Out of 350 people treated only one died—and he was not brought to the laboratory until thirty-seven days after being bitten.

The Pasteur Institute

Pasteur's work on rabies caught the popular imagination far more than his earlier discoveries had done. Fresh honours were heaped on him, and in 1888 the Pasteur Institute was formally opened in Paris. For seven years Pasteur worked there, teaching and experimenting, improving his own methods and explaining them to his pupils. Then he died, at the age of seventy-three, and was fittingly buried in the Institute itself.

There is no better testimony to the work of Louis Pasteur than the history of medical science from his death to the present day. His influence can be detected everywhere. His work on microbes laid an entirely new foundation for the practice of both medicine and surgery; his discovery of the principle of immunity, and its application to the disease of rabies, formed the basis of all modern protective inoculation. Over fifty years after his death his name is still the seal that guarantees the purity of our daily milk.

Rightly has it been said that Louis Pasteur was responsible for the saving of more human lives than any other man in history.

Other Bacteriologists

The science of bacteriology can claim but one chapter in a book of this size, and it is only natural that the bulk of this should have been devoted to the story of its founder, Louis Pasteur. Mention must be made, however, of at least two of the men who achieved so much in this field. Both were Nobel Prize winners, and both died in the present century.

First and foremost was Robert Koch, overshadowed only by Pasteur himself. He was not one of Pasteur's pupils; indeed, there was much keen rivalry between the two. Had they ever been able to collaborate, there is no telling how far their joint researches might have gone. But unfortunately they were separated by a frontier which in 1870 became a battle-ground. As Pasteur said, "Science has no country, but the scientist has one."

Unlike Pasteur, Koch was a doctor. Born in 1843, he had not long completed his training before he was called to serve his country in the war against France. After the armistice he returned to general practice, and began researches in his spare time. He started to study anthrax before this disease engaged Pasteur's attention, and was the first to obtain a pure culture of the bacillus. It must be said that the Frenchman did not neglect to acknowledge his debt to the work of his rival.

In the course of his subsequent researches Koch endowed bacteriology with a carefully worked-out technique. Perhaps the most important of all his work was his method of growing bacteria on solid media, such as plates covered with gelatine. He was a good deal more than a technician, however. He discovered the virus of cholera and, more important still, the tubercle bacillus. Much of his later work was taken up with the study of tuberculosis, and it was his ambition to discover a specific cure for this terrible disease. He did not succeed, nor has anyone yet done so. But his attempts cannot be described

as in vain. If and when tuberculosis is conquered, it need not be doubted that the discoverer of the cure will owe his debt to the pioneer researches of Robert Koch.

The other bacteriologist who must be mentioned was Élie Metchnikoff. Coming from a poor Russian family, he finally came under Pasteur's spell and rose to be his greatest pupil. It was Metchnikoff who discovered the body's natural armour against disease—the leucocytes, or white cells of the blood. He showed how any infection entering the body is immediately attacked by hosts of white cells from the whole neighbourhood, which rush to join battle with the invader like so many trained soldiers. Metchnikoff's discovery threw a new light on the whole subject of infectious disease. It was revealed as a fight between the white cells of the blood and the germs of the disease, which was continued without ceasing until one or the other succumbed.

11

WAR AGAINST GERMS

THE scene was Paris; the occasion, the seventieth birthday of Louis Pasteur. Amid tumultuous applause France's greatest scientist was escorted to the platform by the President of the Republic. Many were the orations that followed, and extravagant the praises; but none of these could have meant more to Pasteur than this simple tribute from an Englishman:

"Truly there does not exist in the wide world an individual to whom medical science owes more than you."

It was not the words that mattered, but the man who spoke them. For what may be taken as a footnote to the last chapter serves also as an introduction to one of the greatest stories in the whole history of medicine.

"The future," asserted Pasteur in his reply, "will belong to those who have done most for suffering humanity. I refer to you, my dear Lister."

Was it any wonder that the assembled crowd went wild with enthusiasm when these two great men embraced each other in the middle of the platform?

It would be impertinent to pass an opinion as to which was the greater. If Lister's work was of more practical value, it depended entirely on the earlier discoveries of the bacteriologist. Listerism, as its founder himself said, was really applied Pasteurism. Happily no thought of rivalry ever entered the mind of either, and they set an example for all time by their superb *entente cordiale.*

Joseph Lister

Joseph Lister was born at Upton, in Essex, on April 5, 1827. His father, Joseph Jackson Lister, was a London wine-merchant with a hobby. The hobby was science, and for his invention of

a new type of microscope he was elected a Fellow of the Royal Society. How far his scientific bent influenced his son can only be assumed, but he must be paid full credit for the good education he gave the boy. Joseph went first to the Quaker schools at Hitchin and Tottenham, and then to University College, London. At the age of twenty he took his B.A. degree, and then started to study for his career, which he had chosen while a schoolboy. He passed to the University College Hospital, where he had already been fortunate enough to witness Robert Liston's first operation under ether, described in an earlier chapter.

Lister gained both his M.B. and F.R.C.S. at the age of twenty-five. Before he had obtained his qualifications, however, he had started on researches of his own. Interested by an eye operation which he witnessed, he was led to investigate the mechanism of the eye, and published a paper on the subject. Another paper followed, this time on the condition of the skin known as 'goose-skin.' Meanwhile, he was becoming more closely acquainted with the terrible diseases that ravaged the surgical wards of hospitals in those times, and already he was pondering on the causes and possible lines of investigation.

Lister's real work, however, was done not in London but in Scotland. In 1853 he paid a visit to Edinburgh, carrying with him a letter of introduction to Professor James Syme, probably the greatest living surgeon of the day, whose work will be discussed in a later chapter. Professor Syme was not only a good surgeon; he was also a shrewd judge of character. Lister had intended to spend only a month in Scotland; in actual fact it was not until twenty-five years later that he returned to work in London. Professor Syme made him his house-surgeon at the Infirmary, and after a year of invaluable experience the young man was promoted to assistant surgeon and also made a lecturer on surgery for the students. By this time Lister had made his home in Edinburgh. He made friends, set up a private practice—and, in 1856, married Agnes Syme, his teacher's eldest daughter.

In the year following his marriage Lister published his first

important paper, entitled "The Early Stages of Inflammation." It contained the results of his observations and researches from his student days, but was based mainly on a series of experiments he had made with the foot of a frog captured at Duddingston Loch. At the same time he was working on the subject of coagulation, or clotting, of the blood, on which a further paper followed a year later. The merit of his work was recognized by his being elected a Fellow of the Royal Society, but his private practice was hardly flourishing. Indeed, about this time his wife was heard to remark with rueful humour of "poor Joseph and his one patient."

Hospitals and Disease

In 1860 Lister was appointed to the Chair of Surgery in Glasgow. His father-in-law, who was largely responsible for obtaining the post for him, regretted his departure; and Lister himself was equally sorry to leave the town that had been his home for seven happy years. But in other respects the promotion was very advantageous. It gave him a wider measure of authority and more freedom for experiment—although he was soon to find that he had to reckon with the Directors of the Royal Infirmary.

Compared with the modern conception of a hospital, Glasgow Infirmary was a terrible place. The first thing that greeted a visitor to the surgical wards was a vile stench, caused by the unchecked suppuration of innumerable wounds. The second noticeable feature was the terrible condition of the patients themselves. It was not their broken bones that caused them so much suffering, but their fevers and wasting. Many of them were dying—nearly all from the same diseases: pyæmia and septicæmia—both forms of blood-poisoning—erysipelas, and, commonest of all, 'hospital gangrene.'

It must not be supposed that Glasgow Infirmary was a particularly bad hospital by the standards of the day. It was worse than Edinburgh, it is true—but then there was only one Professor Syme. Generally speaking, Glasgow may be regarded as typical. The diseases already mentioned were to be found in

every hospital—the larger the hospital, the more prevalent the disease. Hospital gangrene, indeed, was so named because it was found only in hospitals.

The condition of those hospitals was vividly described by Sir James Simpson, who devoted the later years of his life to seeking a solution of the problem. "A man laid on the operating-table in one of our surgical hospitals," he said, "is exposed to more chances of death than the English soldier on the field of Waterloo." He collected and published statistics in support of this contention—and remarkable figures they were. Out of 2098 amputations performed in country practice—that is, in private houses and cottages—226 deaths were recorded; out of a similar number done in hospitals the death-toll was 855—nearly four times the figure! He supported these damning statistics with an analysis of the types of cases concerned, to show that it was not the nature of the amputation that was responsible, but the single fact of the patients being in a hospital.

It is difficult for us to think of a hospital as a breeding-ground for disease—yet that is what it was less than a hundred years ago. To-day cross-infection is comparatively rare, and if a man goes into hospital with a broken leg he does not expect to die of blood-poisoning. A century ago he had little reason to expect anything else. No wonder Simpson called for a reform; no wonder he even demanded that all large hospitals should be pulled down. Thanks to Lister, however, such drastic measures did not have to be taken.

What was the reason for this state of affairs? The answer is simple, yet difficult for us to comprehend.

The hospitals were not clean.

The diseases that caused nearly all the deaths were infectious; and they were unwittingly conveyed from one patient to another mainly by the surgeon himself.

Our idea of a hospital is the embodiment of cleanliness. If we say a thing is 'surgically clean' we are giving it the highest praise we know. But that is simply because we were brought up on Listerism. Lister wasn't. He was brought up to regard cleanliness as a matter of comfort, not of hygiene. To us it is

only natural that a surgeon's hands should be scrupulously clean, that his instruments should be sterilized—because we know about germs, and the connexion between dirt and disease. Lister's predecessors didn't. Bacteriology was only just beginning, and its surgical implications were yet to be discovered.

The correct dress for the operating-theatre in those days was the frock coat. As operating was a messy job the surgeon naturally wore his oldest, and therefore dirtiest, coat. He might wash his hands between operations—but probably only if they felt uncomfortable. He would hardly think of cleaning his finger-nails. The patient's skin might be washed, or it might not; it did not seem to matter much—the wound was almost bound to fester, anyway. The instruments might be washed, or perhaps wiped, or they might just be stuck back in the surgeon's waistcoat pocket. The most convenient place for stitches was the buttonhole of his frock coat. He did not know that his hands, instruments, clothes, the very air itself, were all teeming with bacteria.

We must not blame the surgeon for his ignorance, merely because of our superior knowledge. We must just thank Joseph Lister.

There were always some surgeons who placed a value on cleanliness. Mention has already been made of a few of them, notably the Bishop Theodoric and Henri de Mondeville. They were clean simply because their experience told them that cleanliness gave better results—but they did not know why it should. Professor Syme himself was a good example of this better type of surgeon, and the appalling conditions at Glasgow Infirmary were brought home to Lister all the more strongly by contrast with the comparative cleanliness of Edinburgh. Another 'clean' surgeon was Sir Thomas Spencer Wells, after whom the forceps are named—but he, again, could offer no explanation for the phenomenon, nor did he try to infer any general principles. To such men as these surgical cleanliness was a theory, born of experience, with no apparent scientific basis.

An exception must be made of an Austrian surgeon, Ignatius

Semmelweiss, who did much to reduce the mortality from the dread puerperal fever, commonly suffered by women following child-birth. The American author Oliver Wendell Holmes wrote a paper on this disease, in which he suggested that infection came from the dissecting-room. The same theory was formed independently by Semmelweiss, as a result of his observations that the disease was commonest in the wards attended by medical students, many of whom had proceeded direct from the dissecting-room. "Puerperal fever," he asserted, in 1847, "is caused by conveyance to the pregnant woman of putrid particles derived from living organisms, through the agency of the examining fingers." He put his theories into practice by compelling all students to wash their hands in a solution of chloride of lime before performing such examinations. The results of this simple precaution were remarkable; the mortality in his wards quickly fell from eighteen to three per cent., and later to little more than one per cent.

Semmelweiss made no further advance in antiseptic technique, but had his advice been followed this single contribution would have saved countless lives. Unfortunately his only reward was bitter opposition by 'orthodox' surgeons, who hounded him out of Vienna. He went to Budapest and carried on the good work there, but the enemies he had made would not leave him alone. He finally went mad, and it is sadly ironical to note that a disease he strove to prevent claimed his life as well as his reason; for he died of blood-poisoning caused by a septic finger.

Semmelweiss, as has been said, was an exception. The majority of surgeons, far from practising cleanliness, were proud of their blood-bespattered, pus-encrusted frock coats, and could see no evil in what they termed "a good old surgical stink." Simpson was one of the few who were not satisfied; although he had no doubts as to what was wrong, he could not find the cause of the trouble. It is a matter of regret that this great man, whose contributions to anæsthesia cannot be overestimated, never grasped the truth of Lister's discoveries. When his charges against the hospitals were debated by the British Medical Association in 1869 he dismissed Lister's work

with the remark, "I am rather hopeless of the evils of hospitalism being cured by any such agent as carbolic acid."

Antiseptics

Such were the conditions in hospitals when Lister took up his appointment at Glasgow. It is true that he found little difference between the infirmary and the University College Hospital in London; but then he had been a student, with no responsibility. Now he was in charge.

The first thing he did was to introduce his father-in-law's methods of cleanliness. He made the staff wash their hands before operations, prescribed constant clean dressings on wounds, and gave orders for a good deal more soap and water to be used on the wards. The bills for cleaning-materials rose accordingly, and the Directors of the infirmary expressed their displeasure. They must not be over-criticized. In an age when cleanliness was commonly regarded as a matter of comfort, it was not surprising that such 'luxuries' were discouraged in a public hospital.

At this point it is as well to say something about the background to Lister's subsequent work. In the first place, it must be stated that Lister did not 'invent' antiseptics, nor was he the first surgeon to use them. The word 'antiseptic' comes from two Greek words—*anti*, meaning 'against,' and *septos*, meaning 'putrid.' When it was first coined is not precisely known; but it had found its way into that popular journal the *Gentleman's Magazine* more than a hundred years before Lister went to Glasgow.

The first historical record of the use of antiseptics dates back to the ancient Egyptians. Their method can scarcely come under the heading of medicine, however, as they devoted their art to the preservation of dead bodies only. The Greeks and Romans treated wounds with wine, oil, vinegar, and other preparations, all of very slight antiseptic value. The methods of Ambroise Paré have already been described; and it is clear that he had no more idea than his predecessors of the actual function of antiseptics. It may be said that until the end of the

seventeenth century such antiseptics as were used were intended to relieve pain and to promote healing, but were not connected with the suppuration that was preventing it.

A more scientific approach is to be found in Place's *Hypothetical Notion of the Plague*, published in 1712, which contained the following significant passage:

> As this Phenomenon shows the Motion of the Pestilential Poison to be putrefaction, it makes the Use of Antiseptics a reasonable way to oppose it, and whatever resist and is preservative against Putrefaction and admits not of the generation of Insects . . . are proper and promising Materials to yield Medicine, and for physical preparation against it, such as Cedar, Irish Oak, Cinammon, Spices, and what was used by the Ancients in their embalments of dead Bodies; for the same Vertues that preserve dead Bodies from Insects and Putrefaction, I know no reason why they should not preserve the same Bodies living from the same thing. . . .

About the middle of the eighteenth century Sir John Pringle, whom Pasteur was to refer to as "*le célèbre médecin anglais Pringle*," and whose work with the British Army is described in a later chapter, published a series of papers entitled "Experiments upon Septic and Antiseptic Substances." His work, like that of the Egyptians, was confined to experiments with dead organic matter, but, unlike the work of the Egyptians, was of real scientific value. But it was not until the following century that the real pioneer of antiseptic treatment appeared. This was Agostini Bassi, famous for his study of the diseases of silkworms, who applied his own discoveries in bacteriology to medical practice.

But antiseptics could not be properly understood until the relationship between germs and disease was established. The cause of suppuration of wounds was still unknown. Galen's theory of 'laudable pus' had yet to be disproved, although most surgeons had shared Ambroise Páré's experience that wounds generally healed better without suppuration. But if pus was not always laudable, it was generally agreed to be inevitable. The commonest explanations of suppuration were that pus was formed by the action of the oxygen, or, alternatively, some

undefined 'poisonous miasms,' in the air. Neither theory encouraged further research. A wound caused by an injury was immediately exposed to the air, and an operation could not be performed in a vacuum. If either of these theories was true, therefore, it seemed that nothing could be done about it.

But Lister did not accept the theories. His studies on inflammation and coagulation had led him to form a theory, admittedly incomplete, of his own. Suppuration, he held, was caused by putrefaction. The cause of putrefaction was still a mystery. Lister flatly denied the theory of spontaneous generation, and was of the opinion that putrefaction must be started off by something in the air. What this 'something' was he did not know—but he was firmly convinced it was neither oxygen nor any 'poisonous miasm.' That was as far as he got, until in 1865 a Glasgow friend lent him a copy of a paper that had been published in France two years previously.

The paper was entitled *Récherches sur la Putréfaction.* The author was Louis Pasteur.

Immediately Lister grasped the tremendous significance of Pasteur's discoveries. Putrefaction was a fermentation, due to the presence of living organisms—microbes. Microbes were carried to a wound by tiny particles of dust. Dust floated in the air, and settled on clothes, instruments, and the surgeon's very hands. Germs, not oxygen, caused the process that led to suppuration.

And germs, as Pasteur had shown, could be destroyed.

On more than one occasion Pasteur had lamented his lack of opportunity to apply his discoveries to medicine. It was left to Lister to combine them with the results of his own researches and bring them to their logical conclusion.

Germs could be destroyed. Pasteur destroyed them by heat, but obviously this method was unlikely to be suitable for the treatment of wounds. Lister's immediate task, therefore, was to find a suitable chemical agent which would do the same job. Here he was lucky in having his attention drawn to carbolic acid, which had recently been used with great success in the deodorization of the sewers in Carlisle. Lister went to the town to see for himself, and confirmed that the acid had killed the

bad smell by killing its cause—the microbes. It was the very thing he had been looking for, and he returned to Glasgow ready to start.

It may be mentioned here that when, later, Lister announced his discoveries to the medical world, frequent attempts were made to belittle his work by the charge that he was not the first to use carbolic acid as an antiseptic in surgery. His answer was characteristic; he never pretended he was. That such charges were made gives some idea of the extraordinary lack of understanding that greeted his work. His claim to fame did not rest on such a slender basis as the introduction of a new chemical. He invented an entirely new technique, which was to change the whole practice of surgery. His work has been summed up neatly in four words: he made surgery clean. An idea of the magnitude of this task can be gathered from the foregoing pages about hospital conditions at the time.

Carbolic acid is a derivative of coal-tar, which was used by the Egyptians for their mummies. Another derivative of coal-tar was used in the treatment of wounds by a French surgeon named Demeaux, in 1858, who said that "the action of this disinfectant substance seems to arrest the work of decomposition." Carbolic acid itself was used as an antiseptic by other Frenchmen, notably Jules Lemaire, who wrote a book on it in 1863. "With coal-tar emulsion," he said, "I can arrest and produce at will the formation of pus, as I can arrest and produce fermentation and germination." That Lemaire was working on the right lines is indisputable; but a study of his methods reveals that he had little idea of the correct use of antiseptics—and that he never thought of it as having any purpose other than to destroy bacteria that had already reached the wound. Lister's greatness, as will be seen, lay in his immediate understanding that the ideal use of antiseptics must be to prevent the microbes from reaching the wound.

In actual fact Lemaire's work did not come to Lister's notice until two years after the beginning of his own experiments. The first of these was made in 1865. Typically, and like those that succeeded it, it was on a case of a compound fracture.

Compound Fractures

The essential difference between a single and a compound fracture is that in the latter the skin is broken. In the wards of the Royal Infirmary, Glasgow, it was the difference between a simple healing, on the one hand, and the inevitable suppuration that was so often fatal, on the other. It was this striking difference that had set Lister working on the question of suppuration in the first place.

"I cannot help thinking," he had said, "that the man who is able to explain this problem will gain for himself undying fame."

He was right.

The first case Lister chose was a very severe compound fracture of the leg. The experiment was unsuccessful, the man dying before the results of the new technique could be observed.

The second case was also of a compound fracture of the leg, but of a more favourable nature. The injury was less severe, and the patient—a boy of eleven—in a better physical condition. Lister had the wound dressed with a piece of lint soaked in crude carbolic acid, and then set the bones and splinted the leg in the usual way. After three days without incident the boy began to complain of pain. Fearful of suppuration, Lister removed the splints and dressing—and found a solid scab over the wound. There was no sign of suppuration, and the cause of the pain was revealed as the caustic action of the carbolic acid.

It must be remembered that the carbolic acid which Lister was using was impure and undiluted—no method had yet been found of making it soluble. Modern surgeons would be horrified at the thought of using such a drastic antiseptic on an open wound; but if Lister had had such qualms they might still not be using any antiseptics at all.

Lister removed the dressing, and the wound healed satisfactorily. He had gained his first success. His own comment on the case was typical: "This, no doubt, was a favourable case, and might have done well under ordinary treatment."

The next case was a mixture of success and failure. The patient had been kicked by a horse and sustained a fracture of the leg with a fairly deep wound. The same initial treatment was applied, but this time Lister covered the lint dressing with oiled paper, to prevent the carbolic acid from evaporating. The man experienced no serious pain until a week later, and the cause was again found to be the irritant effect of the carbolic. Under Lister's treatment he rapidly improved until his leg showed only a small sore.

At this point Lister was called away from Glasgow. He was not away long, but by the time he had returned the dreaded gangrene had set in, and in the end the man lost his leg.

Two cases of compound fractures of the arm followed, and with these Lister used a cap of sheet-lead instead of oiled paper as a covering for the dressing. Scabs were formed without suppuration, and both cases healed satisfactorily.

The next two cases were much bigger. In the first a man of twenty-one was injured at work in an iron-foundry, sustaining a compound fracture of the leg with a severe wound; while the second was of a boy of ten who broke his arm in three places and had to have a piece of protruding bone cut off by the surgeon. The treatment was unchanged, except that Lister was now trying tin-foil as a cap for the dressing. Both cases were successful, the only unsatisfactory feature again being the caustic action of the carbolic.

In his eighth case Lister was only partially successful. The patient was a boy of seven who had been run over by a bus, and his leg was in a very bad state. Lister dressed the large, gaping wound all right, but once again he was robbed of full success by an insignificant-looking sore. Gangrene ensued, but Lister caught it in time to save the limb. For nearly nine months he fought the disease with carbolic, and finally conquered it. But he knew that the struggle would never have been necessary had the sore been observed in the first place, and this time he could not excuse himself on the grounds of absence.

Shortly after this Lister published his results in a paper entitled "On a New Method of Treating Compound Fractures."

The paper was based on the work of eighteen months, during which he had applied the antiseptic method to thirteen cases. Two of these had died; two others, described above, contracted gangrene; the other nine recovered without suppuration.

Dressing the Wound

Lister may not have convinced many other people of the value of his antiseptic method, but he had satisfied himself. Carbolic acid was used more and more in his wards, and by the end of three years the mortality following amputations had dropped from forty-five to fifteen per cent.—and the number of amputations necessary was steadily decreasing. During this period the surgeon himself had been directing his energies mainly to the improvement of the new technique.

Before a wound can heal the blood must coagulate and form a scab. Frequently, however, a wound is too large for this to happen immediately, and the tissues are thus exposed to infection from outside. Lister's idea, then, was to create an artificial scab to protect the wound during this danger period.

It has been seen how, from the very first, he began to experiment with different coverings for his carbolic dressing. Now he was to go further, and seek to manufacture something more like a natural scab and incorporating the antiseptic chemical in itself. His first attempt in this direction was what he called 'antiseptic putty,' composed of a mixture of carbolic acid and chalk, the whole being covered by thin metal sheeting. After various experiments with other materials, this was replaced by a 'lac plaster,' a compound of carbolic and shellac.

Lac plaster remained his standard dressing for some time before he was prompted to try a different line of experiment—this time with absorbent materials. He was finally led to gauze, impregnated with an antiseptic. For covering he used at first a mackintosh sheet, and then the absorbent but dust-resistant cotton wool. This final 'artificial scab' has yet to be superseded in the dressing of wounds.

Meanwhile, he was by no means satisfied with carbolic acid in its original state. Its action was too caustic, and from the

first he sought a milder form. Eventually he found it would dissolve in linseed oil, and used one part of carbolic to four of linseed. This was still too strong, however, and it was not until he was supplied with a purer form of the chemical that he felt anything like satisfied. He now found that a solution of one in twenty—and, later, one in forty—was adequately antiseptic, and never again did he pour crude carbolic on to a wound. He who advocated the use of carbolic was the first to realize its dangers, and he was ever warning other surgeons who attempted to repeat his successes by lavish applications of the antiseptic. He sought the mildest possible antiseptic; and, as *The Times* later observed, "his arguments grew stronger as his solutions grew weaker."

The Arrest of Hæmorrhage

After his successes with the treatment of compound fractures Lister began to apply his methods to other forms of surgery. The first of these was with chronic abscesses, and he quickly achieved striking success. Then he turned his attention to an old problem—the arrest of hæmorrhage.

At that time Paré's method of ligature of the arteries was still commonly in use. Silk was tied round the end of the artery, with long ends left hanging loose to provide an exit for the pus that was bound to form; after the knot had rotted through the artery, and a blood-clot formed, the ligature was pulled away. It was clearly an unsatisfactory method, and the obvious improvement that Lister could make was to sterilize the silk with an antiseptic. But that solved only half the problem. For satisfactory healing some way must be found of dispensing with the loose ends. So he sought a medium for ligatures that might be absorbed by the living tissues.

He experimented with silk purged of bacteria, but to no avail. Then he turned to a thread made from sheep's gut, known as catgut, which had been used for ligatures but fallen into disfavour. His first experiment—on a calf—showed that he had found what he was looking for. The gut was absorbed by the tissues, without causing the animal any ill-effects. The only

drawback was that carbolic acid had the effect of softening catgut, so that there was danger of its breaking when the knot was tied. To solve this problem Lister spent long hours on the study of the preparation of catgut, visiting factories and testing various forms of it by himself. It was only after twelve years that he developed the sulphochromic gut that was ultimately adopted in surgery.

Return to Edinburgh

New discoveries inevitably attract young men rather than their seniors, and the early scepticism of the established surgeons of Lister's times was only to be expected. All the more credit, therefore, is due to the greatest of these for his immediate recognition of the value of the younger man's discoveries. Professor James Syme, who had taught Lister surgery, was one of the very first to try out his son-in-law's antiseptic method, and once he had proved its merit to his own satisfaction he determined not to rest until it was universally accepted. Unfortunately, however, the campaign was barely started when the Professor had an apoplectic stroke. He recovered, but was compelled to resign from the Chair of Clinical Surgery at Edinburgh. At least he did not have to worry about the ability of his successor, for it was fittingly Lister himself who filled his place. And it was characteristic of Lister that, in his opening address to the students, he should say of Professor Syme, "As I have the privilege of free access to his inexhaustible store of wisdom and experience, he will, in some sense, through me be still your teacher."

Lister was not sorry to leave Glasgow. He had met with only obstruction and ill-feeling from the Directors of the infirmary, who had shown anything but pride in the work he had done there. Nor were they alone in their hostility. Throughout the profession acknowledgment was rare and criticism widespread. The first major recognition of Lister's work came neither from Scotland nor from England, but from the continent. Dr Saxtorph, Professor of Surgery at Copenhagen, read Lister's papers and considered them sufficiently important for him to

pay a special visit to Scotland to see the surgeon at work. On his return to Denmark Saxtorph applied his newly gained knowledge to his own wards, and a year later he was able to write to Lister, saying, "I feel so much indebted to you for what I have learnt in seeing you employ the antiseptic methods that I thought it my duty to let you know how things went on in my hospital practice; and I am happy to say that I have never tried any innovation which answered so admirably as this treatment of wounds."

At the same time Lister's publications were attracting attention in other continental cities, notably in Germany; and before long tributes were coming in from all parts of Europe. Only in his own country was he still without honour; and his task was well summed up by the words of a famous patient of his, the poet Henley:

> We hold him for another Heracles,
> Battling with custom, prejudice, disease.

While Dr Saxtorph and other foreign surgeons were proving the efficacy of Lister's methods the British Medical Association was assembled in solemn conclave to hear one of his own compatriots proudly state that "during the last three years, since the antiseptic treatment has been in vogue, I have not allowed one of my patients to be treated with carbolic acid." Even Sir James Simpson himself had thrown the great weight of his influence into the battle against antiseptics, which was all the more regrettable in the light of his own earlier struggles against custom and prejudice.

Lister never allowed himself to be drawn into controversy unless he could help it. To most of the attacks his only reply was the publication of fresh evidence in favour of his methods. Personal reputation never worried him; he was anxious that his technique should be known and practised only because he believed it was correct.

Lister never ceased to preach that the antiseptic method could only be successful when used on the basis of Pasteur's theories, and his very first lecture at Edinburgh was devoted

entirely to a demonstration of these. If people were going to understand his own technique, he considered, they must first have a thorough grounding in the basic principles on which it was based. Incidentally, it was while he was at Edinburgh that he started to correspond with Louis Pasteur, thus beginning a friendship that culminated in the scene described at the beginning of this chapter. Eighteen years before that occasion, he had written to Pasteur thus:

> Allow me to take this opportunity to tender you my most cordial thanks for having, by your brilliant researches, demonstrated to me the truth of the germ theory of putrefaction, and thus furnished me with a principle upon which alone the antiseptic system can be carried out.

Meanwhile, he was still improving on that system, and it was his later work that raised him head and shoulders above men like Jules Lemaire. From the beginning he regarded antisepsis, or the destruction of germs in the wound, as only a step towards the true ideal—asepsis, by which the germs are prevented from ever reaching the wound. Surgery to-day is based entirely on aseptic principles, and careless statements have been made about Lister's methods having been superseded. Nothing could be further from the truth. They have been brought nearer to perfection, but the fundamental principle is unchanged.

The weapons in the battle remained the same, with carbolic acid, in various solutions, always predominant; but the battleground shifted—from the wound to its surroundings, to the surgeon and his assistants, to his instruments, to the very air itself. Prevention is better than cure, and it was prevention that Lister was seeking.

It has already been seen that Lister was always a comparatively clean surgeon, thanks largely to the early influence of Professor Syme. Once he had discovered the reason for cleanliness he never tired in his quest for completely aseptic conditions. Carbolic acid was used on the patient's skin; it was used for the washing of the surgeon's hands and those of his assistant's; above all, it was used for the sterilization of instruments. But

this was not enough. Pasteur had proved that bacteria lived in the air, and whatever other precautions were taken, nothing could save the tissues from being exposed to the air during operation.

So it was that Lister devised the carbolic spray, by which the bacteria in the air were attacked throughout the operation by a solution of carbolic acid. It was first worked by hand, then by foot, and finally by steam. Other surgeons adopted it, especially on the continent, where Listerism had made such good progress. There was, however, no definite proof of its efficacy, nor had Lister been able to demonstrate its actual effect on the teeming bacteria in the atmosphere. It was only natural that doubts were expressed, and it was even suggested that if used carelessly it might even have the effect of driving bacteria into the wound.

Lister was a great man. He never regarded his own theories as foolproof, and he was ever ready to accept genuine criticism. He went into the question with his usual thoroughness, and accepted the results of his investigations, unpalatable as they were. He found, in the first place, that the destruction by this means of all the bacteria in the air was impossible; and secondly, that the danger of infection from the air was very slight compared with that from contagion of the surgeon's hands and instruments. So he finally abandoned the spray, and advised other surgeons to follow suit. He did not spare himself in self-criticism. "I feel ashamed," he declared, "that I should have ever recommended it for the purpose of destroying microbes in the air."

While Lister was seeking more and more to eliminate the sources of infection he was applying ever weaker preparations to the wound itself. The nearer he approached to aseptic conditions, the less was the need for antiseptics. It was this fact that so many other surgeons failed to grasp. Impressed by Lister's success with carbolic acid, they read only half the story; and he was constantly warning them that they must not, as he put it, "expect carbolic to act like a charm." Even more significant was a remark he made in the year following his return to Edinburgh. "Of all those who use antiseptics in surgery,"

he said, with justifiable pride, "I suspect that I apply them least to the wound."

In this brief account of Lister's work at Edinburgh mention must be made of one other innovation he made in surgical technique. This was the introduction of indiarubber tubing to allow the escape of discharge from a wound. The discharge started after an operation on an axillary abscess, and Lister took this measure when fever had developed owing to lack of proper drainage. It was a daring experiment, and so successful that the method was quickly adopted and is still in use to-day.

It is not usual for medical historians to mention the names of patients, but an exception must be made in this case. For the subject of Lister's experiment was none other than Queen Victoria.

Final Recognition

While Lister was at Edinburgh he was visited by many foreigners and few Englishmen. The address that was most conspicuous by its absence on the visiting-cards was London, where antiseptic methods were scarcely practised at all. True, they had been tried; but few of the operators had seen Lister at work, and hardly any understood the underlying principles of the technique. Many, as has been said, thought antisepsis merely meant the use of carbolic acid, and left it at that. Others were still unconvinced of Pasteur's theory of germs, and, as Lister said, "without this guiding principle many parts of the treatment would be unmeaning . . . failure on the part of those who doubt or disbelieve it is therefore only what I should expect."

Then, in 1877, Lister was offered the Chair of Surgery at King's College, London. The news of the appointment met with much out-spoken criticism in the capital; and in Edinburgh seven hundred students signed a petition imploring Lister to stay. But, much as he regretted leaving Scotland, he knew which way his duty lay. London must be convinced—not for the sake of the surgeons, but for the patients who were still dying of erysipelas, blood-poisoning and hospital gangrene.

Lister's first address in London was on exactly the same lines as his first lecture in Edinburgh. He explained and demonstrated Pasteur's theory of germs. The reception, however, was rather different. He was not speaking to students alone, and the eminent surgeons in his audience afterwards made it clear that they wanted more practical proof than that.

They soon got it. Where he could not convince by words Lister dispelled all doubts by his deeds. The sceptics watched him operating, saw the results, and were converted. The attitude of the more generous was well expressed by the greatest of them, Sir James Paget. While he was working at St Bartholomew's one of his junior colleagues was a disciple of Lister's, although a far less skilful surgeon than Paget himself; and Sir James had the grace to say:

> . . . it makes me look back to that part of my life with remorse, and I may say that either through ignorance or inattention I had a mortality of which he could justly say he would be utterly ashamed. He has, during all these operations, used antiseptic treatment thoroughly; and his success has been so great, in contrast with my failures, that I cannot for a moment doubt its value.

Later Years

Lister remained at King's College for fifteen years. In the latter part of his life he made several foreign tours, notably to France, Germany, Hungary, and America. He was created a baronet in 1883, and other honours followed. In 1891 he was one of the founders of the British Institute of Preventive Medicine, in London, modelled on the Pasteur Institute in Paris, and later renamed the Lister Institute of Preventive Medicine. In 1893 he left King's College, and in the same year he suffered a terrible loss in the death of his wife, Agnes, who had helped and encouraged him throughout his most difficult times.

In 1895 he became President of the Royal Society, a distinction which he retained until 1900. In 1896, when he retired from practice, he was elected President of the British Association; and a year later he achieved the distinction of being the

first representative of medical science to be raised to the peerage. He was awarded the Freedom of the City of Edinburgh in 1901; and in the Coronation Honours of the following year he was one of the original members of the newly instituted Order of Merit, and sworn a Privy Councillor at the same time. King Edward, who had just recovered after his famous operation for appendicitis, paid him a well-phrased tribute at the time. "Lord Lister," he said, "I know well that if it had not been for you and your work I would not have been here to-day."

In the same year, at a banquet of the Royal Society given in Lister's honour, the American Ambassador said, "My Lord, it is not a profession, it is not a nation, it is humanity itself which with uncovered head salutes you."

But his health was giving way, and the rest of his life he lived mainly in retirement. He died in 1912, at the age of eighty-five; and as the annual report of the Royal College of Surgeons said, "His work will last for all time; its good results will continue throughout the ages; humanity will bless him evermore, and his fame will be immortal."

Appreciation

It is impossible to exaggerate the importance of Lister's work. Pasteur discovered the greatest single cause of disease; Lister armed humanity against it. The change that surgical practice underwent during his lifetime was nothing short of a revolution—so much so that the history of surgery is now generally divided into two distinct periods: before and after Lister. An idea of the limitations in the former period may be got from the words of Sir John Erichsen, a very distinguished surgeon under whom Lister worked in his early days in London. "The abdomen, the chest, and the brain," asserted Sir John, "will be for ever shut from the intrusion of the wise and humane surgeon."

Reference has already been made to later improvements in aseptic methods. One of the most important of these was the introduction of gloves for the surgeon to wear when operating. Sterilized cotton gloves were used at first, and in

1890 Professor Halstead, an American surgeon, introduced rubber gloves, which were quickly adopted by the profession. Another great innovation was the use of caps, gowns, and masks by the entire theatre staff. Gauze masks were first used in the Charing Cross Hospital in London in 1900. Methods of sterilization, meanwhile, had undergone considerable changes. The use of chemicals was largely replaced by boiling, which is both surer and quicker, although sharp instruments are still sterilized in carbolic acid, as is catgut. Carbolic acid is no longer used on the patient's skin; the normal preparation for operation consists of shaving, where necessary, followed by cleansing with surgical spirit and painting with iodine. Gauze, impregnated with flavine or some other mild antiseptic, is still the commonest dressing.

The methods have been improved, but the principles remain the same. For the safety of the operating-table and hospital ward to-day all credit must go to Lister.

So tremendous were the results of Lister's work in antisepsis that his other qualities are usually forgotten. Chief of these was the fact that he was, above all, a first-class practising surgeon, and he made several notable contributions to general surgical technique. He also invented new instruments, and improved on the method of administering chloroform.

But inevitably it is for his discovery of the antiseptic system that Lister will always be remembered. As a fitting epitaph, here is a verse addressed to him by one of his German followers, Stromeyer:

> Mankind looks grateful now on thee
> For what thou didst in surgery,
> And Death must often go amiss
> By smelling antiseptic bliss.

12

MAN AGAINST MOSQUITO

"I WAS and am a hero-worshipper, and Manson and Laveran were my heroes. . . . Let the cup of gratitude flow over rather than be stinted."

Thus wrote Ronald Ross. His generous tribute gives us a glimpse of the character of this strange scientist who seemed to love the arts more than science, but surely loved humanity more than either. For it was love of humanity that spurred him to devote his life to one of the oldest riddles in the history of medicine—the problem of malaria.

The Scourge of the Tropics

Of all the diseases in the world probably none has caused more sickness and death than malaria. One reliable authority has gone so far as to estimate that malaria has been the direct or indirect cause of over one-half the deaths of all mankind throughout history. This cannot, of course, be proved; but it gives some idea of the extent of the suffering that has been brought about by this single disease.

The fact that malaria is now regarded mainly as a tropical disease is in itself a triumph. For it was not always so; it has inflicted a heavy toll on Europe, and England itself has suffered some terrible epidemics. The Ancients knew it to their cost, and, of course, the Greeks had a word for it. They believed it had been brought to Europe from Egypt, where it was known to be widespread. Hippocrates wrote quite a lot about malaria, and he noted its prevalence near marshes and its seasonal outbreaks. He and other Greek physicians studied the symptoms and made careful case-notes, but there is nothing in their records to suggest that they ever suspected its true cause. Its importance in ancient history cannot be disputed, and it is regarded as more than probable that malaria was one of the

main factors leading to the decline of both the Greek and Roman civilizations.

The Time-honoured Treatment

Oddly enough, the correct treatment of the disease was established while the cause was still a matter of conjecture. At least three hundred years ago the Indians of Peru were treating their sick with a powder prepared from cinchona bark. How this first came to be brought to Europe is not precisely known. A legend subsequently sprang up round the alleged miraculous cure in 1640 of the Countess del Cinchon, wife of the Viceroy of Peru, and she was said to have introduced the drug to Spain; it is a good story, but probably untrue. All we know for certain is that it was about this time that European doctors first heard of cinchona bark, and that it was certainly used to great effect by Sir Thomas Sydenham in the malaria epidemic that ravaged England in the same century.

It was from cinchona bark that the alkaloid quinine was eventually extracted, and this was the only known treatment for malaria until very recent times. Chemistry has now given us others, synthetic preparations, the best known of which is mepacrine. This is used as a prophylactic as well as for ordinary treatment—that is, for prevention as well as cure. People going into regions where malaria is rife are dosed with mepacrine in advance, just as they might be vaccinated or inoculated.

Other drugs besides mepacrine have been synthesized, the most important of which was announced as recently as 1945. This was paludrine, or, to give it its exact formula, N^1-p-chlorophenyl-N^5-isopropylbiguanide! Paludrine was claimed to be more powerful than any other anti-malarial drug yet prepared, but it has since been challenged by two American wartime productions—chloroquin, or resochia, and the compound known as SN 13276. Which of the new drugs will prove most effective in the end has still to be decided.

The Discovery of the Cause

The word 'malaria' is a simple combination of two Italian words meaning 'bad air.' It was given this name because it was believed to be caused by the breathing of the unwholesome air given off by marshes. It was a natural assumption, based on the proved fact that the disease was commonest in marshy regions.

But malaria is not caught from a germ floating in the air. It is caused by what is known as a parasite, a living organism which takes nourishment from the human body and gives nothing in return. So far as we know this was not even suggested until 1846, when a scientist named Rasori formed the opinion that the disease might be caused by such a parasite which reproduced at fixed intervals, according to its species. Rasori could advance little evidence in favour of his theory, which was thus only a very good bit of speculation.

In the following year the parasite of malaria was actually seen in the human blood without being recognized, by a pathologist named Meckel. Included in his observations was a description of the characteristic black pigment, or colouring, which always accompanies it.

The credit for the real discovery of the parasite must go to the earlier of Ross's two heroes—Alphonse Laveran. While serving in Algeria as a Medical Officer in the French Army, in 1878 Laveran definitely identified it as an animal parasite in the red corpuscles of the blood. Under the microscope he noted the increase of pigment and, most important of all, the appearance of tiny, wriggling, filament-like forms known as 'flagellæ,' on which the whole course of Ross's subsequent researches depended.

Laveran's discovery was taken a step further by Camillo Golgi, one of a number of Italian scientists who were working on the problem of malaria at the same time. In 1886 Golgi first differentiated between the two common types of the disease—tertian, in which the fever occurs in cycles of forty-eight hours, and quartan, where the fever recurs every

seventy-two hours. Golgi also noted that each bout of the fever came after an increase of spores from the parasite in the blood.

The cause of malaria was discovered, but the problem was by no means solved. Now that it was known that the disease was not brought by a germ carried in the air, but was due to the presence of a parasite in the blood, the question naturally arose—how did the parasite get there?

The Rôle of the Mosquito

The mosquito was under suspicion before anything was known of the true cause of malaria, simply because where there was malaria, there were always mosquitoes. Thirty years before Laveran's discovery Dr Josiah Nott, an American, gave it as his opinion that both malaria and yellow fever were transmitted by mosquitoes. He could not furnish much evidence in support of his theory, nor could Louis Daniel Beauperthuy, who later suggested that malaria was caused by the injection of a venomous fluid by mosquitoes, on the same lines as snake-poisoning. The theory was repeated by David Livingstone, who recorded in his *Missionary Travels* that "African Fever," as he called it, followed the bite of the insect. In his *Narrative of the Expedition to the Zambesi* he was more explicit, writing that "myriads of mosquitoes showed, as probably they always do, the presence of malaria."

But while the cause of the disease was unknown these theories were only good guesses. And from the writings of the Hindu physicians of the fifth century it would seem that the same guesses had been made a very long time before. It was only after Laveran's discovery that any real scientific theory could be advanced.

The first to put forward such a theory was an American named King, who published in 1883 nineteen reasons for assuming that malarial poisons were brought from marshes by mosquitoes, and passed to human beings through their bites. In the following year Laveran himself declared his belief in the mosquito theory, although he again could offer little fresh

evidence. Robert Koch, who was investigating malaria at the same time, worked on the same theory, but without practical success. So it was left to the other of Ross's two heroes, Patrick Manson, to expound the theory which, in Ross's own modest words, "so accurately indicated the true line of research that it has been my part merely to follow its direction."

Manson's interest in malaria sprang from his own discoveries in connexion with another tropical disease, elephantiasis. This also is caused by a parasite in the blood, known as filaria; and in 1877 Manson proved that it was conveyed from one human being to another by the mosquito. Laveran's discovery that malaria also was caused by an animal parasite naturally led Manson to consider the possibility of a similar means of transmission. Before the details of his theory are given, however, something must be said about the man who finally proved its truth.

Ronald Ross

Ronald Ross became a doctor against his own inclinations. Born in Almora, in India, on May 13, 1857, as a youth he showed a marked artistic bent; and had it not been for the influence of his father, an Army General, it is doubtful if he would ever have taken up medicine as a career. Never was parental guidance so strongly vindicated!

He began his studies at Bart's in 1874, and was undistinguished as a student. He completed his training and gained his degrees—but still found time to write poetry and play the piano. Finally he came seventeenth out of twenty-two passes in the examinations for the Indian Medical Service, which he entered in 1881.

Ronald Ross as a young man was a problem. Of undoubted intellectual ability, he showed such a diversity of interests that it must have seemed at one time as if he would never be anything but a brilliant dabbler. Apart from his interest in poetry and music, he wrote novels, devised original systems of shorthand and phonetic spelling, studied mathematics and invented a new

system of geometry, and entered the realm of astronomy and philosophy. As he himself said, he needed several lives to satisfy all his varied ambitions; and in the next twelve years he gave every indication of satisfying none—frittering away his talents in a dilettante fashion, a square peg in a round hole.

The round hole, of course, was medicine, which as yet had no place on the agenda of his ambitions.

This was the most significant fact in the life of Ross. It was no mere desire for scientific knowledge that impelled him to tackle the problem of malaria. The motives that eventually made him begin his researches sprang from a far nobler source. He was not interested in science for science's sake; medicine to him was not an end, but a means. Ever since boyhood he had been vaguely seeking the end: to do something for humanity. Ironically, it was only as a last resort that he turned to his own profession for the means.

It was no chance clinical observation, but the sight of human suffering, that prompted Ross to start his great work. It was estimated that 1,300,000 people in India died of malaria every year, and an idea of the prevalence of the disease may be gained from the fact that this figure represented less than one per cent. of the total number infected. Of the 300,000 British troops in the country no less than 100,000 were admitted to hospital for malaria every year. It was the sight of the patients in the hospital wards that moved Ross to write:

> The painful faces ask, can we not cure?
> We answer, No, not yet; we seek the laws.

So, after twelve years of routine duties in the I.M.S., he began to seek the laws in earnest.

He could count on little assistance from officialdom. As a junior officer he was not encouraged to show initiative. Illustrating the attitude of mind among officers in the Dominion at that time, he told a good story about how he once proposed to his Adjutant in Bangalore that the tubs in which mosquitoes were breeding should be emptied. The Adjutant turned down

the proposal on the grounds that it would be "upsetting the order of nature"!

As has been said, the starting-point of Ross's research was Laveran's discovery of the malarial parasite. News of this had reached India, and in 1892 Ross wrote to England for Laveran's books. Meanwhile he was examining blood-specimens to try to find the parasite himself. He did not succeed, and at first he was inclined to doubt the Frenchman's conclusions.

The Turning-point

In 1894 Ross returned to England on furlough. On his arrival in London he did two things: arranged for the publication of a novel he had written, and went back to Bart's to see what he could find out about malarial research. He was referred to Dr Manson, and in April of that year began not only one of the most fruitful collaborations in the history of medicine, but a friendship that was destined to last a lifetime.

At last Ross saw the malarial parasite—in Charing Cross Hospital! Manson showed him the various forms of the organism in blood taken from a patient there, and Ross doubted Laveran no longer. Seeing his interest and enthusiasm, Manson began to tell him of his own theories. It was while the pair were walking down Oxford Street that the older man said casually, "Do you know, I have formed the theory that mosquitoes carry malaria just as they carry filariæ."

Dr Manson explained his theory more fully. He attached great importance to the fact that the filament-like 'flagellæ' emerged only after the blood had been taken from the human body. Nature does everything with a purpose; so the only reason for this appearance of these queer little organisms must be that the parasite was intended to continue its existence outside the human body. But how did the parasite get out of the body, and where was its existence to be continued? The only answer to this, said Manson, was some bloodsucking insect. And since the parasite of elephantiasis was carried by a particular species of mosquito (the culex), it was reasonable to suppose that the same might apply to malaria.

About the manner in which the parasite entered the human body Manson was less certain. He thought the infection was probably carried by drinking-water, on which the mosquitoes had died and shed their parasites. He also suggested food might be contaminated in a similar way.

When Ross embarked for India again in March, 1895, he was a changed man. He had found his mission in life at last, and his mind was made up. He could not rest until he had solved the problem of malaria. Indeed, he was so enthusiastic and impatient to start work that the ship had scarcely set sail before he began pricking the fingers of his fellow-passengers, in the hope of finding some of the parasites. This was a habit that clung to him, and when he landed in India he used the same method for getting specimens from the natives—at a cost of a rupee a prick!

Ross's immediate aim was clear. He had seen the malarial parasite in the blood of a human being; now he wanted to find the same parasite in the body of a mosquito. So as soon as he returned to duty at Secunderabad he started a private 'mosquito farm,' obtaining his stock by capturing the insects and also breeding them from larvæ. Meanwhile he studied the blood of malarious patients under a portable microscope of his own invention, and as soon as he detected a parasite he tried to persuade one of his own mosquitoes to bite the patient. For the first time he learned that mosquitoes can be shy when it comes to biting—or, as he put it, "as obstinate as mules." Perhaps with good reason; for once the mosquito had consented to bite, it was killed and placed under the microscope, for dissection and examination of its stomach, where Ross believed the parasite lived.

The difficulty, of course, was to find the species of mosquito that carried this particular parasite. There Ross was completely in the dark. There are something like 2000 species of mosquitoes, and it might be any of the numerous varieties that haunted malarious regions. The only thing to do was to go on trying till he found the right one. Ross realized this from the start, and he was undismayed by the magnitude of his self-

imposed task. But he was much less patient with the obstacles placed in his way by officialdom. As it was, he had to continue with his routine duties, and could only carry out his investigations in his spare time. He did not expect assistance from the authorities, but more than once he was moved to complain bitterly against what seemed almost like deliberate official obstruction.

However his superior officers might frown on Ross's 'irregularities,' one person at least never lost faith in him. In his regular letters of encouragement and advice Dr Manson made it clear that he regarded his friend's work as of the very highest importance. He told Ross to consider himself as Sir Galahad looking for the Holy Grail.

The correspondence between the two scientists makes fascinating reading. There was nothing dry about Ross's accounts of his experiments. However technical the subject, he was always human and often humorous. The following is an extract from a letter describing his observations through the microscope of a free flagella in a drop of blood, and its reactions to what are known as phagocytes, which act as the policemen of the blood. It sounds a dull subject—but this was how it appeared to Ross:

> He [the flagella] brought up against a phagocyte and remained so long that I thought the phagocyte had got hold of him. Not a bit; he was not killed or sucked in; but kept poking him in the ribs in different parts of the body. I was astonished; and so, apparently, was the phagocyte. He kept at this for about a quarter of an hour, and then went away across two fields and went straight at another phagocyte.

After he had been watching for fifty minutes, along came a third phagocyte

> with his mouth open right and straight across the field, but had no sooner got near him when the flagellum left his fallen foe and attacked the new one, holding on and shaking like a snake on a dog. In one minute the third phagocyte turned sharp round and ran off howling!!!—I assure you. I won't swear I heard him howling, but I *saw* him howling.

Ross was in the middle of his work when the first major interruption occurred. There was a sudden outbreak of cholera in Bangalore, and he was transferred there for sanitary duties, which occupied him more than a year. He heard the news of the transfer with dismay, but eventually it proved less of a setback than it seemed at the time. The time was not wasted. It enabled him to gain unique experience of practical sanitation which was to stand him in good stead in later years, when he was working on the prevention of malaria. Also, although his research-work was interrupted, it was not broken off completely. He continued his examination of the various species of mosquitoes, and formed the conclusion that the culex variety was probably not the one he was seeking. In addition, he began to doubt the latter part of Manson's theory—that the parasite was transmitted from the insect to human beings via drinking-water. As yet he could offer no proof, but he was becoming increasingly convinced that the parasite went back to man by the same way it had come out—through the bite of the mosquito.

He finished his duties in Bangalore in 1897, and was granted two months' leave. As a holiday resort he chose the most malarious jungle he could find, and, not unexpectedly, was himself stricken with the disease. Judging from his remarks, he seemed almost pleased about it. He gave the parasite what he described as "a warm reception" by dosing himself with quinine, and then got out his microscope and calculated the number of parasites in his own blood and the time they took to breed.

When his leave was over Ross asked for an extension in order to continue his researches. It was, of course, refused, and he was ordered back to Secunderabad. As enthusiastic and energetic as ever, he continued his investigations in off-duty hours right through the long, hot summer, until the month of August.

On the twentieth of that month Ross's efforts were at last rewarded, and for the rest of his life that date was solemnly celebrated as 'Mosquito Day.'

The Culprit Discovered

The morning of that memorable day was uneventful. Mosquitoes were dissected as usual, with the usual negative results. At one P.M. Ross was on the last of the batch. He killed it, cut it open, and—

Within a matter of seconds he knew that his search was at an end. There, in the muscle-fibres in the tiny stomach-walls of the insect, were the cells of the parasite—not only the cells, but also the unmistakable black pigment with which he was so familiar. His quarry had been tracked down. The carrier of the malarial parasite was at last identified—as the species of mosquito known as 'anopheles,' a Greek word meaning 'harmful.'

To-day the anopheles mosquito is notorious. Its graceful, slender body, its dappled wings, its peculiar attitude in standing, with its body in one straight line at an angle to the surface on which it is resting—this is the description that has been more widely circulated than that of any other criminal, 'wanted'—by the medical police. Not all the anopheles family carry the parasite, however, as Ross later discovered; and it must not be forgotten that it is only the female of the species that carries it at all.

In his description of the discovery Ross wrote, "The Angel of Fate fortunately laid his hand on my head." It has been described by smaller minds as yet another of science's frequent 'accidents'—an accident by which the scientist, after years of unrewarded investigation, after the dissection and examination of something like a thousand mosquitoes' stomachs, at last discovered what he had been looking for all the time!

Ross's first action was to submit specimens to his two heroes, Laveran and Manson. Then he got back to work—but the problem was not yet solved. He had tracked down the guilty anopheles, but he still had to find the truth about the manner of transmission of the parasite. True, he was more than half-way. Now, for the first time, he could see the mysterious flagella in its true colours—as a male sperm of the malarial

organism, wriggling about in the mosquito's stomach in search of a female cell to fertilize.

Ross had discovered the identity of the carrier, and he had traced the progress of the parasite from the human blood to the stomach of the mosquito. The question that remained to be solved was how it was conveyed to another human being. Was it, as Manson thought, by means of drinking-water? Or was it by the insect's bite?

And just as Ross was beginning to seek the answer to this question, he received the following order:

"Under instruction from Command Headquarters, Bombay, Surgeon Major R. Ross, I.M.S., will proceed immediately to Bombay for military duty."

Ross had put up with a lot, but this was too much. He protested, told the authorities how far he had got with his researches, and begged to be granted facilities to complete his work. The answer to his application is memorable. It read: "I don't understand what this officer means. He was sent to this Command by H.E. the C.-in-C., and there he will remain until H.E. orders him away."

In December of the same year Ross's account of his discovery was published in the *British Medical Journal*, while the discoverer himself was languishing in Kherwara, a tiny station isolated in the wilds, devoid of the malarial specimens that he so urgently needed. The injustice of this cavalier treatment angered Manson, who at once set to work in London to get the decision reversed. He was now working at the Colonial Office, and by his influence he finally managed to get Ross's case heard. Thus in the following January his friend was ordered to Calcutta for full-time research. This time, however, the authorities had gone to the other extreme; he was ordered to investigate not only malaria, but another tropical disease, the mysterious kala-azar, as well—and given six months' for both tasks! It was very flattering, as Ross drily observed, but an unfair burden. He asked to be relieved of research-work in connexion with the second disease, but to no avail; the best he could do was to get permission to tackle malaria first.

It was in Calcutta that Ross administered the death-blow to the second part of Manson's theory. In the absence of suitable human malarial specimens he continued his work on a similar parasite found in birds, which had been discovered by a scientist named Danilewski as long ago as 1885. Ross was interested only in the part of the parasite's life-history that was spent in the mosquito, and by following the various changes undergone in the stomach-wall he finally traced the progress of the parasite via the salivary gland to the mouth. It was as he thought; the parasite went back to man by the same way it had left him—by the bite of the mosquito. "Men and birds don't go about eating dead mosquitoes," he wrote to Manson. "No, Nature is far too clever for such an attempt. She brings the mosquito (and the infection) straight to the man or bird and puts it nicely into his blood, so as to give it every chance."

As a proof of this Ross fed mosquitoes on sparrows already diagnosed as malarious. After a week the parasites were in evidence in the salivary glands of the insects, which were then allowed to bite healthy sparrows. After another week the blood of the latter was examined, and out of twenty-eight birds used for the experiment twenty-two were found to be infected.

"Hence I think I may now write Q.E.D.," Ross told Manson, "and congratulate you on the mosquito theory indeed."

And to Laveran he wrote:

"Will you permit me to conclude with an expression of satisfaction that, after three years' labour, I am at last able to make this announcement to you, who not only originated our correct knowledge of this subject, but from the first divined that the mosquito is connected with the propagation of these parasites."

Laveran's congratulations followed quickly; and it was Manson's honour to announce his colleague's discovery to the British Medical Association in July of that year.

The Final Proof

It was always a sore point with Ross that he did not have the chance to be the first to demonstrate the true facts about malaria in human beings. He was prevented from doing so only because he was kept on research on kala-azar, and it fell to other scientists to work out the life-history of the human malarial parasite. This was achieved by a team of Italians led by Giovanni Grassi in the same year—but after the publication of Ross's work on the parasite in birds.

It was unfortunate that these Italian scientists omitted to pay due acknowledgment to the results of Ross's researches, of which they must have availed themselves, as their own work was merely the logical conclusion of his original discoveries. As Manson said to Ross, "You have forged the key, the others must take the trouble to open the door."

Ross, however, was less tactful. He protested vigorously against what he termed "scientific piracy"—and was duly reproved by the *British Medical Journal.* There was some controversy on the matter, from which Ross, supported by Manson, Lord Lister, and Robert Koch, finally emerged victorious. That his grounds for complaint were justified is not in doubt, although it has been suggested that the unpleasant dispute might have been avoided had he been less outspoken. But it would be difficult to blame a man who was himself so scrupulously careful to acknowledge the work of other scientists.

Although Lord Lister, then President of the Royal Society, was one of the first to acclaim Ross's discoveries, it was some time before they were generally accepted. The 'bad air' theory died hard; and it disappeared only in 1900, when Manson supplied proof too conclusive to be questioned. He arranged for two British doctors to go to Italy and live throughout the malaria season in a mosquito-proofed hut in the Campagna, near Rome. At the end of the season they were both in perfect health. At the same time Manson proved the converse by importing infected mosquitoes from Italy and allowing them to bite two volunteers, both healthy young men who had never

suffered from the disease. Both contracted malaria, fortunately without any serious results.

The name of the first of these volunteers for the cause of medicine was P. Thorburn Manson, the son of Dr (afterwards Sir) Patrick Manson.

Ross's Later Work

It has already been seen that Ross's first interest in malaria sprang from his heart rather than his head. If further proof of his humanitarianism were needed it would be sufficient to point to his career after he had achieved his aim. Having found the cause of the disease, it did not take him long to decide upon the only effective remedy. Man could never be completely protected against mosquito-bites; anopheles mosquitoes were too numerous to be wiped off the face of the earth; therefore the only solution lay in the systematic removal of their breeding-grounds. In two years, said Ross, an efficient sanitary service could stamp out malaria in every city and large town in the tropics. But he did not leave it at that; temporarily abandoning the microscope, he devoted his energies to the study of preventive measures.

In 1899 he retired from the I.M.S. and took up a post at the Liverpool School of Tropical Medicine. In the summer of the same year he went to West Africa—notorious as the 'White Man's Grave'—to see the sanitary situation for himself. He made certain recommendations to the authorities there, but after his return to England it became clear that they were not being implemented. Two years later, therefore, he organized a private expedition, consisting of himself and one assistant, and, equipped with pick-axes, shovels, oil, cement, and creosote, returned to West Africa to show the local authorities how it should be done, whether they wanted to know or not. "It was sanitary Bolshevism," he wrote gleefully.

In the following year Ross was invited by the French Suez Canal Company to undertake a similar mission to Ismailia, in Egypt. He accepted, and as a result of his work the incidence of malaria in that town dropped from 1551 in 1902 to nil in 1906.

Ross remained at Liverpool till 1912, and it is pleasing to know that his work did not pass unrewarded. He was elected Fellow of the Royal Society in 1901, awarded the Nobel Prize for Medicine in 1902, and knighted in 1911. During the War of 1914–18 he was given the post of Consultant in Malaria, and he went with the R.A.M.C. to Egypt, Gallipoli, Salonika, and Italy. For these services he was awarded the K.C.M.G. But the recognition that must certainly have pleased him more than any of these honours was the foundation in 1926 of the Ross Institute and Hospital of Tropical Medicine.

However hard he had to work on medicine, Sir Ronald never lost his early interest in the arts, especially literature. Apart from his famous memoirs, he published poems, novels, plays, and critical prose, as well as books on mathematics.

He died in September 1932. No more fitting epitaph could be found than the words of *The Times* obituary notice:

"He slew the dragon and delivered mankind from immemorial bondage."

The Results

It would be idle to pretend that Ross's hopes have been anything like fulfilled. Much has been done, but more remains to be achieved. To-day it is estimated that over 800 million people, or over one-third of the population of the world, suffer from malaria; while the annual death-rate from the disease still amounts to approximately three and a half million. These are terrible figures.

Ross was to some extent justified when he ascribed the failure to wipe out malaria to official slowness and unwillingness to spend public money. Even so, he must have realized the enormous difficulties in securing co-operation from native populations. In Europe malarial control has proved remarkably effective, and the same applies to other territories under European administration or influence. Hong Kong and Singapore are good examples; and in Palestine, Jewish immigrants who settled in the most malarious districts of the country to-day enjoy a far greater freedom from the disease than the native

Arab communities. But in the larger territories of West Africa and India sanitation is only in its infancy. Swamps have been drained, pools covered with oil, and ponds stocked with fish that feed on the mosquito-larvæ; the discovery by Dr G. C. Ramsay of the anopheles mosquito's need for sunshine has been followed up by the planting of thousands of miles of hedges to screen off breeding-grounds; but the widespread practice of flooding fields for irrigation is a tremendous obstacle to really effective control.

The most spectacular result of Ross's work was in the construction of the Panama Canal. Ferdinand de Lesseps, famous for his achievement of the Suez Canal, tried to cut a similar waterway at Panama, but gave up the project owing to the prevalence of the twin mosquito-borne diseases of malaria and yellow fever. It was the American W. C. Gorgas who organized the sanitary measures that finally enabled the canal to be constructed, and when it was completed (in 1914) the area was practically cleared of both diseases. Gorgas did not forget to give credit where it was due. "It seems to me not extreme," he wrote to Ross, "to say that it was your discovery that enabled us to build the canal on the Isthmus of Panama."

The most recent advance in malarial prevention is the use of the new chemical known as D.D.T. (dichlore diphenyl trichloroethane), which has the effect of paralysing the jaws of mosquitoes so that they cannot bite. It was used with great success by the Fourteenth Army in the Burma Campaigns of the War of 1939-45.

Malaria the Medicine!

A note must be added about a very strange aspect of malaria. It is difficult to imagine that any good could come from a disease with such a record; yet malaria itself has been effectively used in the treatment of other diseases. It was Dr Jauregg, of Vienna, who observed that certain chronic mental conditions showed improvement after attacks of malaria; and the disease was subsequently induced by means of injection, and then

treated with quinine in the usual way. Good results were achieved, especially with cases of general paralysis. The cause of this phenomenon was later interpreted as the effect of the high temperature produced by malaria, rather than the disease itself, and treatment was modified accordingly.

13

THE GOLDEN AGE

FOUR chapters of this book have been devoted to the discoveries of the nineteenth century, yet the story of this Golden Age of medicine is still not complete. So great was the progress of the science that it would need a whole volume to cover the period adequately. The present chapter, therefore, is intended to give just a brief outline of some of the main advances that have not already been covered.

Surgery

The discoveries of Lister inevitably dwarf every other advance in surgical practice, but the work of his predecessors, as well as that of his followers, demands consideration. Chief among the former were two Scotsmen, both of whom have already been mentioned: Robert Liston and James Syme.

Liston and Syme were friends and colleagues as young men, and for some time they worked together and helped each other with their cases. Apart from a passionate interest in surgery, however, they had little in common. Liston was six feet tall, well built, with tremendous muscular strength; Syme, small, of less than average physique, looked insignificant beside him. The difference went further than that. Liston was brusque in manner, impatient, ever sure of himself, while Syme was quieter and more thoughtful. It was not surprising that such a difference should lead to a quarrel, which was to be dragged on for seventeen years, but happily ended in a complete reconciliation.

This quarrel was no doubt prolonged by the surgeons' respective supporters, for it was an obvious temptation to lesser men to take sides in this struggle between the two greatest surgeons of the day. Liston was of the type that wins quick popularity. He openly gloried in his physical strength, and

his skill in the operating-theatre became almost legendary. He used the knife quickly and surely, and was never at a loss to improvise. He scorned such adjuncts as the tourniquet, claiming that his left hand was good enough to stop the flow of blood while his right hand performed the operation!

If Liston was naturally popular, Syme was the sort of man who commands respect. Like his son-in-law, he was careful and therefore tireless in his efforts. He took a longer view of surgery than Liston did, aiming at a permanent improvement in technique rather than individual achievements. He preferred the considered judgment to the swift decision. But when it came to action he worked quickly and surely. Although less spectacular than Liston, he never undervalued the importance of speed in operating. The anæsthetic was yet to be discovered; incisions had to be made in the flesh of a fully conscious patient, and then every second was sheer agony. Professor Syme also spent more time in lecturing and writing papers; and his friend and assistant, Dr John Brown, the author of *Rab and His Friends*, summed up his three activities: "he never wasted a word, or a drop of ink, or a drop of blood."

Lister made the methods of all his predecessors look crude by comparison, and Liston and Syme could not be excepted. Had they been born in the antiseptic era there is no doubt that their results would have been incomparably better. When one considers the conditions under which they worked the marvel is that they achieved so much. Each of them performed operations that had previously been regarded as impossible, and their contributions to surgery were great.

Mention must also be made of the greatest of the London surgeons of this time—Sir James Paget, who has been noted only as an early opponent and subsequent supporter of Lister's antiseptic method. He was a fine surgeon, a great teacher, and deserves to be remembered most for his discovery of the terrible bone-disease named after him. A full account of his life and work, and that of his London colleagues, unfortunately lies outside the scope of this book.

After Liston, Syme, and Paget came Lister, and all subsequent

surgery of any importance was based on the antiseptic method. Part of the story—the gradual trend to aseptic conditions—has been told; the other part concerns the introduction of operations hitherto too dangerous to be attempted, and the consequent growth of specialism within surgery.

The abdomen was the first part of the body to be explored in this new era, and it was characteristically one of Lister's German followers, Theodore Billroth, who was prompted by the Englishman's discoveries to make medical history by removing a cancer of the stomach. Billroth introduced several other new operations, notably on the intestines. The problem of appendicitis, meanwhile, was being investigated afresh, especially in the United States. It was an American surgeon who performed the first successful appendicectomy, or removal of the appendix; and the operation gained considerable attention in England when Sir Frederick Treves removed the same organ from King Edward VII in 1902.

Another 'forbidden territory' before Lister was the brain. In 1884 Lister's nephew, Sir Rickman Godlee, first removed a tumour from the brain, and three years later a tumour was successfully removed from the spinal cord. A new branch of medicine had arisen, to be known as neurological surgery, or simply neuro-surgery.

The thyroid gland was excised; bones were plated; a radical cure was found for inguinal hernia; the gall-bladder was removed—these, and many other operations that the previous generation had deemed impossible, were performed safely and surely . . . thanks to Lord Lister.

Famous Physicians

To include all the important physicians of the century in this chapter is impossible. The steady progress made since the Renaissance was greatly accelerated, and famous doctors were practising all over Europe and in America. As with the surgeons, therefore, a selection must be made; and it is suitable to confine this to three very distinguished physicians who all worked at the same hospital—Guy's, in London.

What Liston and Syme were to surgery, so were Bright and Addison to medicine—except that there is no record of their ever having quarrelled. Each secured a permanent place in the annals of medical science by the discovery of an important disease; and to-day Bright's Disease and Addison's Disease hold honoured places in every medical text-book.

Both graduated at Edinburgh—Richard Bright in 1813, and Thomas Addison two years later. Bright had a strong inclination for travel—as a student he joined in an expedition to Iceland which nearly cost him his life. After obtaining his degree he toured the continent, and recorded his observations in a travel-book which he himself illustrated. He was interested in nearly everything, and it was not till later that he devoted his full energies to his profession. Nevertheless, he was only thirty-one when he was appointed assistant physician to Guy's.

By this time Addison had come to the famous hospital, and his ability quickly attracted attention. When, four years later, Bright was promoted to full physician, he was succeeded in his former appointment by his junior colleague. The pair did much of their work together, and they collaborated to write a book called *The Elements of Practical Medicine*, which contained, among other things, the first correct account of appendicitis.

While they pooled their ideas in this work and shared the task of lecturing on medicine each was making his own individual contribution to the science. Most of Bright's work was connected with the investigation of the kidneys, and it was as a result of this that he discovered the disease that bears his name. Thanks to his literary style and gift for art he was able to enrich medical literature with a number of books and papers that were to prove of tremendous importance to succeeding physicians. Bright's Disease, of which nephritis is the most usual form, is, after heart disease, the commonest cause of death in Great Britain; and it was recently described as the "most important medical problem of the day."

Addison, meanwhile, specialized mainly on diseases of the chest, although the disease that was named after him concerned the suprarenal gland. His own name for it was "Bronzed

Skin," on account of its most striking characteristic, and his description of its discovery tells that he "stumbled upon" it while investigating anæmia. Actually, as a result of these researches he had the honour of giving his name to two diseases, although the other of these, 'Addison's Anæmia,' is now more generally known as pernicious anæmia.

In 1837 Addison was raised to the same level as his colleague by his appointment to full physician. Bright retired in 1843, thus bringing to an end one of the greatest partnerships in medical history, which had lasted unbroken for over twenty years. Addison remained at Guy's for a further seventeen years. Then, despite a deputation from his students begging him to stay, his health forced him to resign his post. He died in the same year; and it was some time before the importance of his work was fully realized.

The third of the great physicians associated with Guy's was Sir William Withey Gull. Born in 1816, the son of a barge-owner, he educated himself as a pupil-teacher and went to Guy's as an apprentice at the age of twenty. Four years later he was a Bachelor of Medicine, and in 1846 he took his doctorate. From being appointed lecturer this one-time apprentice rose eventually to full physician, attended the Prince of Wales for typhoid fever, was made a baronet, and left over £300,000 when he died.

Gull made no striking discoveries. He was a clinician rather than a scientist, and it was in the treatment of disease that the value of his work lay. It was he who started the crusade against the indiscriminate administration of drugs that was in vogue at the time. "There is a belief amongst the poor," he said, "that disease is caused by Providence and is cured by drugs." But it was not the ignorance of the poor that angered him; it was the way in which that ignorance was traded on. "Whilst you put up a public house at one end of your street and a provident dispensary at the other," he said caustically, "how can you expect your people to be healthy?" He did not spare his own profession. On one occasion, when called in by another doctor for consultation, he made a rapid diagnosis of heart-disease;

the doctor, who doubtless had heard stories of Gull's acid tongue, hastened to apologize for having overlooked the clinical signs. "Never mind, it is just as well," was Gull's scathing reply; "for if you had detected it, perhaps you might have treated it!"

Gull laid down three main rules for the treatment of disease. First and foremost was rest; second, the careful and sparing administration of such drugs as were really useful; and finally, good nursing. "Nursing," he asserted, "sometimes a trade, sometimes a profession, ought to be a religion."

Few modern physicians would find much to disagree with in Gull's principles.

Claude Bernard

The son of a vine-grower, Claude Bernard started life as an assistant in a chemist's shop. He was an ambitious lad, however, and while still in his teens composed a vaudeville comedy, *La Rose du Rhône*. This brought him some local fame and a little money. Encouraged by his success, he wrote a full-length play, gave up his job, and went to Paris to make his fortune.

Things did not turn out quite like that, however. The eminent critic who read his play told him gently but firmly that he might do better as a doctor than as a dramatist. Claude took his advice, and medicine was the richer. Twenty years later he became the first Professor of Physiology at the Sorbonne University; ten years after that he successfully asked Louis Napoleon for a research laboratory; and when he died, at the age of sixty-five, he was the first French scientist to be given a State funeral.

Bernard is best remembered for his exposition of the "experimental method," in which he laid down a set of principles that are still accepted as the basis of medical research. One, at least, of his sayings must be quoted: "When entering a laboratory one should leave theories in the cloakroom."

It is to Claude Bernard that we owe the basis of our knowledge of the digestive system. In his time the process of digestion was thought to begin and end in the stomach. Bernard proved the

error of this theory. "Gastric digestion," he wrote, "is only a preparatory act." He traced digestion to the intestines, and showed that the biggest share in the process belonged not to the stomach at all, but to the secretion of the pancreas, or sweetbread.

Most of his experiments were performed on animals, which he obtained as best he could. The animals did not always share his interest in the experimental method, and were ever on the look-out for a chance to escape. So it was that on one occasion he had to face the wrath of no less a personage than a police inspector, whose dog had found its way home with a piece of Bernard's apparatus in its abdomen. Happily the scientist was able to remove the offending apparatus, and as the dog was none the worse for its adventure he managed to mollify the inspector even to the point of friendship.

One of Bernard's greatest discoveries was glycogen, or animal starch—the fuel on which the body depends for its heat and energy. This led him to a theory that altered the whole face of physiology. The body, he showed, could build as well as destroy; it was not just a 'bundle of organs,' each with independent functions, as had for so long been believed.

Although recognized by his fellow-countrymen, Claude Bernard was a prophet without honour in his own family. His wife, more worldly than he, did not understand why he would not turn his brains from the laboratory to the more lucrative private practice. In the end she left her husband, taking their two daughters with her, and Claude spent the rest of his life alone save for a housekeeper. His friends were not numerous; but the few he had esteemed him highly. And the greatest of these was Louis Pasteur.

A New Science

Erasistratus of Alexandria is believed to have been the first to suggest a difference between sensory and motor nerves, and Galen of Pergamos was the discoverer of the sympathetic nervous system. But it was Charles Bell of Edinburgh who founded the science of neurology.

Bell began his career as an anatomist, and he was the first man since Leonardo da Vinci and Vesalius to appreciate the true relation between anatomy and art. As a student under his brother, John, he began to publish illustrated books on the subject; and when he came to London at the age of thirty it was as an artist rather than as a Member of the College of Surgeons of Edinburgh that he achieved renown.

He took a house in Leicester Square and taught anatomy to a mixed audience of students in medicine and art. The artists were in the majority at first, but after a few years he began to arouse interest in medical circles. In 1814 he was appointed to the staff of the Middlesex Hospital, and in the following year he went to Brussels to help to deal with the casualties from the battle of Waterloo. There he operated for fifteen hours a day, until, in his own words, he was "powerless with the exertion of using the knife."

Meanwhile, his anatomical studies had led him to explore the structure of the brain. In 1807 he had published his famous *Idea of a New Anatomy of the Brain*, which was the starting-point of his later researches in the workings of the nervous system. "What I hope to prove," he said, "is that there are two great classes of nerves." He proved this beyond all doubt; and on his discoveries is based the whole of the science of neurology.

The nervous system may be likened to a modern telephone service. Incoming calls represent the sensory nerves—those that convey messages, mainly from the skin, through the spinal cord to the brain. Outgoing calls represent the motor nerves—those that convey orders from the brain, again via the spinal cord, to the muscles. The telephone exchange, of course, is the symbol for the brain and spinal cord, which together form what is known as the central nervous system.

Bell discovered a great deal more than these vital facts. He made an exhaustive study of the nerves in all parts of the body, and communicated his findings in papers read to the Royal Society. These were later given a permanent form in his book *The Nervous System of the Human Body*. His fame spread, and when

he visited M. Roux in Paris, the French professor dismissed his class by saying, "*C'est assez, messieurs; vous avez vu Charles Bell!*"

The next major contribution to the study of the nervous system was made by a physiologist named Marshall Hall. Another Edinburgh student who achieved success in London, his fame would have been secure if only for his work in stamping out "the slaughterous practice of blood-letting"—a form of treatment that boasted a pedigree of over thirty centuries. He defined the lancet as a "minute instrument of mighty mischief."

But it was the discovery of what is known as the reflex action that was Hall's greatest achievement. He began his researches at the age of forty-two, and, according to his own calculations, spent 25,000 hours of his spare time on it. His patience was well rewarded. To return to the illustration of the telephone service, a reflex action may be compared with the automatic dialling-system. The message is still carried by the sensory nerve, but only as far as the spinal cord; there it is short-circuited to the motor nerve, which carries orders to the muscles without any instructions from the brain. A reflex action, therefore, is spontaneous and involuntary. A good example is the reaction to a pin-prick in the sole of the foot. A sensory nerve conveys the news to the spinal cord, and without further ado a motor nerve carries back instructions for the foot-muscles to contract, thereby removing the foot from danger. The whole process takes only about one-thirtieth of a second.

Later in his career Marshall Hall performed a great service to humanity by originating the method of artificial respiration that has saved thousands from death by drowning.

Charles Bell and Marshall Hall laid the foundations of neurology, and their work was carried a stage further by Claude Bernard. The Frenchman discovered the vasomotor nerves, which are largely responsible for the regulation of the supply of blood to the various parts of the body.

These three discoverers were anatomists and physiologists, and so far only the structure and functions of the nervous

system had been considered. The study of its diseases followed. Foremost among the early neurologists were two other Frenchmen, Guillaume Duchenne and Jean-Martin Charcot.

Duchenne was born in Boulogne-sur-mer in 1806, the son of a sea-captain. His father wanted him to be a sailor, but he made up his mind about his career while still a boy. At the age of nineteen he went to study in Paris, one of his first teachers being René Laënnec. He was a Doctor of Medicine at twenty-five, and he set up in practice in his home town. About this time the recently discovered Faradic current was coming into vogue for the treatment of chronic rheumatism, and Duchenne saw in this a means for studying the normal action of the muscles. He became so absorbed in these new researches that he eventually gave up his practice, and, at the age of thirty-six, took his battery to Paris, where he spent the rest of his life on this study. He had no official appointment, and wandered in and out of the hospitals in a most unconventional way. At the age of sixty-one he published the results of his work in a book entitled *Physiologie des Mouvements*. He made the important observation that muscles do not act singly, but in groups, and this and other discoveries enabled him to describe several muscular diseases that had never before been diagnosed. He died in 1875, largely unrecognized; and it was some years later when the value of his work was appreciated.

More famous than Duchenne was Jean-Martin Charcot, whose work also was done in Paris. In 1862 Charcot was appointed Physician to the Salpêtrière Hospital, which he finally made the first neurological centre in the world. Charcot's main work was on hypnosis, which he regarded as an artificially created hysteria. He and his pupils were largely responsible for the establishment of neurology as a separate medical specialty.

The Magic Camera

"Possibly even, by the concentration of electrical and other lights, we may render many parts of the body, if not the whole

body, sufficiently diaphanous for inspection by the practised eye of the physician or surgeon."

The man who made this prophecy was Sir James Young Simpson, who died in 1870. In 1895 the X-ray was discovered.

The discovery was made by one man, and it was, for once, a true accident. That does not excuse the strange assortment of legends that persisted long afterwards, whose only aim seemed to be to belittle the achievements of the discoverer. Most popular of these was the 'key and book' story, which ascribed the discovery to the result of a photographic plate being accidentally left under a book in which a latch-key was used as a bookmark. There is not a word of truth in the story, and the real facts are as follows.

The X-ray was discovered by Wilhelm Conrad Röntgen, a German physicist, on November 8, 1895. Röntgen was fifty years of age at the time, and he had held the Chair of Physics at Würzburg for the preceding ten years. He was a research-worker as well as a lecturer, and his investigations were concerned with the cathode ray. He was experimenting with a Crookes' tube, observing the effect of sending an electrical discharge through a high vacuum. On the day in question he was working in a perfectly dark room, and his tube was completely covered with black cardboard. Switching on the current, he was suddenly aware of a bright light shining in the room, a short distance away from where he was working. He stopped his experiment, and found that the glow was coming from a small piece of paper coated on one side with barium platino-cyanide, which happened to be lying near the Crookes' tube. He switched off the current, and the light disappeared.

"What did you think?" he was asked later.

"I did not think. I investigated," replied the scientist.

There was nothing accidental about Röntgen's subsequent discoveries. Some hitherto unknown rays had passed through the black cardboard enclosing the Crookes' tube, and he immediately set to work to find out more about them. Switching on the current again, he picked up the piece of coated paper and turned it over, so that the barium platino-cyanide was facing

away from the tube. It still glowed! Next Röntgen tried the effect of interposing various opaque objects between the tube and the paper. A thousand-page book, he found, did not obstruct the rays, nor did two packs of cards. Deal boards, an inch thick, might almost have been transparent, for all the effect they had. Was there nothing, then, that would obstruct these rays?

Fortunately there was, otherwise medical science would have gained little from the discovery. A single layer of tinfoil cast a very slight shadow; several thicknesses of the same substance had a more noticeable effect. Other metals, even in thin sheets, offered a much stronger resistance. These are termed radio-opaque, and the most important is lead, which has proved of unrivalled value in X-ray insulation.

Röntgen's most striking experiment was with his own hand. Placing it between the tube and the paper, he saw the bones clearly outlined in the form of dark shadows. This was the first indication of the value the rays were to have as an aid to medical diagnosis. Next came the discovery that the rays, although invisible to the human eye, affected photographic plates. The impression recorded is best described not as a photograph, but as a shadow which varies in density according to the length of exposure and the radio-opacity of the substance interposed.

Röntgen frankly admitted that he knew nothing about the nature of the rays whose properties he had observed, and he gave them the name of X-rays after the algebraical symbol of the unknown. Two months after his discovery he announced his findings to the world in a paper entitled "*Über eine neue Art von Strahlen*," or "On a New Kind of Ray." In the following month he gave a demonstration to scientists, and he had the happy experience of being one of the few discoverers to have his work accepted without serious opposition. However incredible the claims in his paper might have appeared, the very nature of his demonstration made scepticism impossible. One could hardly disbelieve the evidence of one's own eyes.

The importance of the X-ray to medicine was realized at once.

Bones could be examined while the skin was still intact, a fracture could be diagnosed in an instant, and with the aid of an X-ray plate an almost perfect union could be achieved. On the same principle the new ray was to be of tremendous value in the diagnosis of all diseases of the bone, and especially in dental surgery. Nor was that all. The fact that most metals were in some degree radio-opaque made it possible for foreign bodies to be observed in the human body without operation. When a child swallowed a pin, for example, its course could be followed right down the alimentary canal. A bullet embedded in a soldier's body could be similarly located without the use of a probe.

The value of X-rays in diagnosis was by no means exhausted with this. Within little more than a hundred years medical science had been enriched by three great aids to diagnosis: Auenbrugger's discovery of percussion, Laënnec's stethoscope, and Röntgen's X-ray. The first two were especially valuable for their use in the diagnosis of tuberculosis in the lungs, and it was fitting that the X-ray should eventually come to be used more for this than for any other purpose.

Meanwhile, in the year following Röntgen's discovery a scientist named Becher began to investigate the possibilities of X-raying various organs of the body by the use of what are termed 'contrast media.' The stomach, for example, is not radio-opaque; but by filling the stomach of a guinea-pig with a solution containing lead Becher was able to obtain a clear shadow of the walls of the organ on a photographic plate. Later, certain drugs, notably bismuth and barium, were found to be just as opaque to X-rays as lead, and without any toxic effects on the body. They were introduced into the stomach and duodenum by swallowing; the walls of these organs were then clearly outlined, and the X-ray could detect the presence of an ulcer. Bismuth is no longer used for this purpose, but the most common medium is still barium meal.

Still the story of this magic ray is not told. Soon after it was brought into general use it was discovered to be dangerous as well as useful. Early radiologists, unaware of its peculiar

powers, lost their limbs and even their lives by constant exposure to the rays. One of the greatest of these martyrs was Dr J. Hall-Edwardes, of Birmingham. He began using the X-ray only a year after it had been discovered, and later developed ulcers on his hands which did not respond to ordinary treatment. He realized the cause—but carried on with his work. Only when he had had both his hands amputated was he forced to retire. To-day, happily, such danger to operators has been largely overcome by a careful system of insulation, although vigilance is still very necessary.

One of the diseases caused by X-rays was cancer of the skin. When medical science, ever ingenious, came to turn the rays' destructive properties to a beneficial purpose, cancer was one of the first diseases to be attacked. For if the rays could burn healthy tissues, they could also burn diseased ones; the property that killed could also cure. Thus the X-ray came to be used for treatment as well as for diagnosis, and it proved especially effective on skin diseases, such as ringworm. The treatment of malignant growths is more difficult, owing to the increased danger of harming the healthy tissues surrounding them. It is this 'deep X-ray therapy' that present-day investigators are seeking to improve.

Following upon recent atomic research, tests have been made of the action of neutrons on living tissues. These experiments have yielded some encouraging results. Neutrons have been shown as approximately four times more effective than X-rays in destroying malignant growths, and only three times as potent against normal tissues. Although these researches are still in an early experimental stage, it is conceivable that in time X-rays may be replaced in treatment by neutrons.

Radium

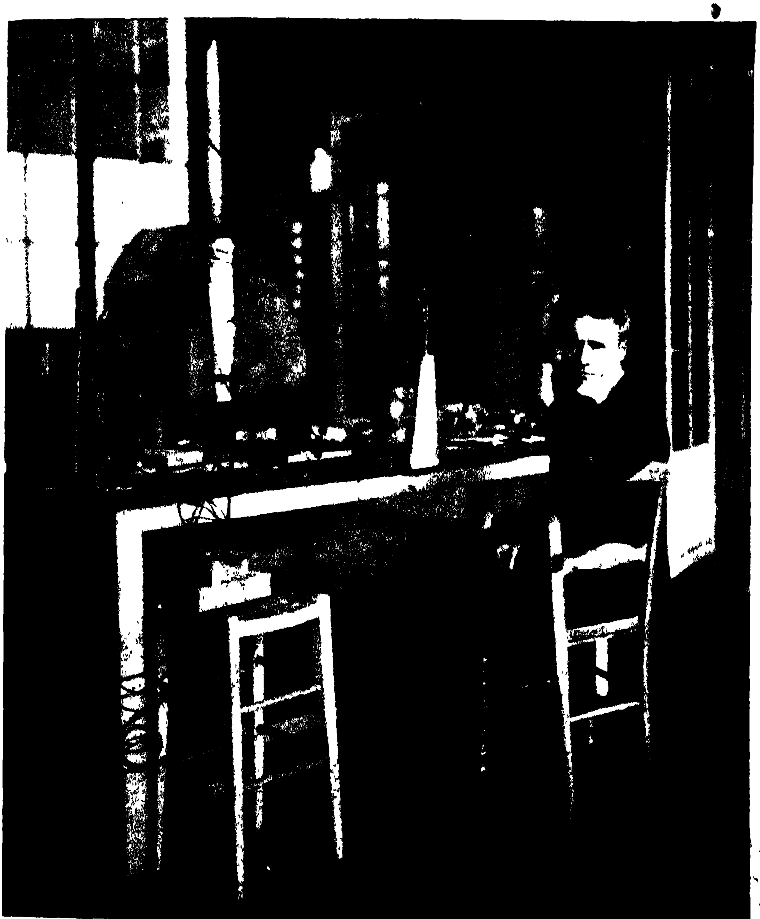
No modern scientific discovery captured the imagination of the public more than radium. The story is a romance in more senses than one. It is the story of brilliant deduction, incredibly hard work, and the mutual love and devotion of husband and wife.

The full story of Pierre and Marie Curie belongs to the Romance of Chemistry and Physics rather than to the present volume. Fortunately it has been told many times, and even found its way into the cinema. The idea of radium came from Marie; Pierre gave up his own researches to join her in the quest, and from that moment their work was inseparable. Nor did they ever give outsiders a chance to separate their respective contributions. Nearly all their writings were in the first person plural, and there was no means of assessing the individual merits of one or the other until Pierre's tragic death in a street-accident in 1906. After that Marie carried on the work so successfully that she became the most famous woman in the world. Her death in 1934 was, in a sense, more tragic than Pierre's; it was caused by her own gift to humanity—radium.

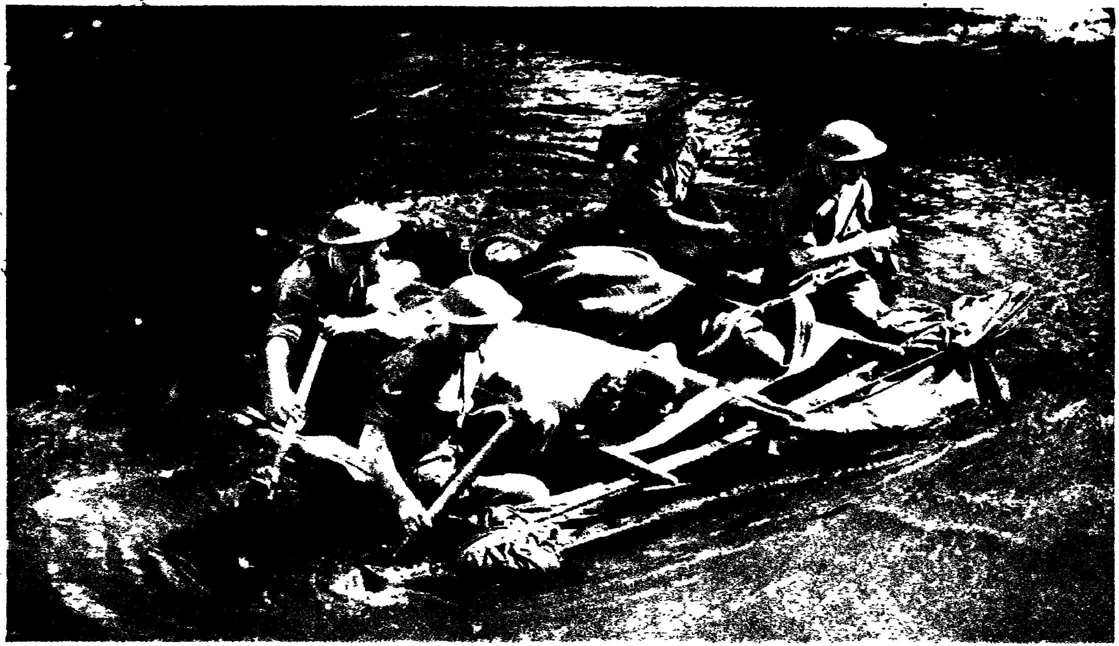
Röntgen discovered the X-ray in 1895. In the following year a French physicist, Henri Becquerel, observed the phenomenon of radioactivity. In 1898 radium was discovered, and after four more years of intense labour one decigramme of the substance was extracted by the Curies. As early as 1900, however, some of the peculiar properties of radium had been observed, including its power of burning the skin. This interested Pierre, and after exposing his arm to its action he was overjoyed to see a nasty lesion appear. Like the X-ray, radium could burn living tissues; and again this harmful property was turned into a practical means of treating disease. 'Curie-therapy,' as it was called, was introduced in the treatment of tumours and certain forms of cancer. It has proved especially successful in the treatment of cancer of the lip and tongue; deep X-ray therapy, however, is more suitable for deeper growths and more distant tumours.

The discovery of artificial radioactivity in 1934 stimulated physicists to produce new radioactive substances, and one of these—known as radio-sodium—is, weight for weight, ten million times more active than radium itself! Its toxic effects appear to be relatively slight, and radio-sodium may play a large part in the treatment of malignant growths in the future.

Cancer is one of the remaining unsolved mysteries of medicine. Neither cause nor cure has yet been discovered, and it is the subject of extensive research to-day. Meanwhile, the X-ray and radium are doing much to hold its ravages in check.



MARIE CURIE IN HER LABORATORY



FERRY AMBULANCE: THE R.A.M.C. IN ACTION

14

ROYAL ARMY MEDICAL CORPS

MILITARY medicine has existed as long as armies, which is a very long time indeed. Homer spoke of the good work done by military surgeons in the Trojan Wars, and it has been proved that the Romans had medical officers attached to their troops, although they carried only non-commissioned ranks. In the Middle Ages, however, army doctors were mainly civilians; mention has already been made of the experience gained by these war surgeons, who included such famous men as John of Arderne, Richard Wiseman, and Ambroise Paré.

Physician-General to the Forces

The modern British Regular Army came into being in the seventeenth century, and the medical care of troops was entrusted to a Physician-General. The most famous of the holders of this appointment was Sir John Pringle, who has aptly been called the "Father of Military Medicine." Born in 1707, he was educated at St Andrews and Edinburgh Universities, and then went to Amsterdam to study the world of commerce. While in Holland he chanced to visit the town of Leyden, where he had the good fortune to hear Dr Boerhaave lecturing. Pringle was so impressed that he at once gave up the idea of a business career and enrolled as one of Boerhaave's pupils. Among his fellow students was Gerhard van Smieten, with whom the Scot formed a lasting friendship.

Pringle took his M.D. in 1730, and went to Edinburgh to practise. He proved a good doctor, and in 1742 he was appointed physician to the Earl of Stair, who was Commander of the British forces in the Low Countries. At the same time Pringle became physician to the Military Hospital at Flanders, and he served with the troops throughout the campaign.

One of the most far-reaching results of Pringle's work with the army came from his suggestion to the Earl of Stair that arrangements be made with the enemy for the protection of hospitals on both sides. The Earl communicated the proposal to the Duc de Noailles, and the French Commander readily accepted it. "This agreement was strictly observed on both sides during that campaign," Pringle wrote later, "and though it has since been neglected, yet it is still to be hoped that on future occasions the contending parties will make it a precedent." More than a century later this 'gentlemen's agreement' was embodied in the Geneva Convention, which introduced the sign of the Red Cross.

In 1744 Pringle was appointed Physician-General to the Forces. He served with the Duke of Cumberland's troops in the '45 Rebellion, at the end of which he settled down in London. The succeeding years he spent mainly in improving the conditions in military hospitals and barracks. He had observed that both nurses and patients seemed to have a horror of fresh air, and he commented that the air in unventilated wards became "corrupted." Although he lived long before the germ theory of disease and the antiseptic method, Pringle's own scientific researches had led him to understand something of the nature of infection and the importance of ventilation and cleanliness.

> As to the disposition of hospitals [he wrote], with regard to preserving the purity of the air, the best rule is, to admit so few patients into each ward, that to those unacquainted with the danger of bad air, there may appear room to take in double or triple the number. . . . I have generally found those rooms the most healthful where, by broken windows and other defects, the air could not be excluded.

Among his other reforms was a set of rules of hygiene for military establishments, in which he sketched out plans for camp sanitation, ventilation, and the general preservation of health.

In 1752 Pringle published his book *Observations on the Diseases*

of the Army, which included the results of his military experience and suggestions for reform. He was appointed physician to the Queen in 1761, and created a baronet five years later. Eventually he rose to become physician to King George III and President of the Royal Society.

The Crimean War

After Pringle's death military medicine was largely neglected. While the science was advancing by leaps and bounds, its practice in the Army lagged behind. There was no proper medical organization, and when the Crimean War broke out the Army Medical Department was found to be totally unprepared for the medical care of troops.

In the face of tremendous difficulties the few medical officers did their best, and when the Victoria Cross was inaugurated in 1856 one of the first to receive the honour was a war surgeon named James Mouat, of the 6th Dragoons. The text of the award ran as follows:

> Major Morris, 17th Lancers, was lying wounded in a very exposed position in front of the enemy, after the charge of the Light Brigade: at great personal risk Mouat went to him, dressed his wounds, and thereby saved his life.

The "Lady with the Lamp"

Nursing, in the early nineteenth century, was not considered a very respectable occupation. The female nurse, as Dickens vividly portrayed, was an inferior sort of domestic servant. It was little wonder, therefore, that when Florence Nightingale told her mother she wanted to take up nursing the reception was anything but favourable. "It was as if I had wanted to be a kitchen-maid," she said later. Florence was of a well-to-do family and had had a genteel education, so every effort was made to deter her from 'degrading herself' to such a lowly status.

But her mind was made up. In secret she studied nursing and hospital conditions, and during holidays on the continent she took the opportunity of visiting hospitals and nursing-homes

wherever she went. She found one notable exception to the general rule about nursing—in establishments run by religious orders. The only good nursing was done by the Catholic and Protestant Churches.

In spite of the opposition of her family Florence eventually took a post as superintendent of a Harley Street nursing-home. She remained there for about a year. Then the Crimean War broke out, and within a short time reports came in of the appalling conditions in the military hospitals at Scutari. The public was alarmed. "Are there no devoted women among us," wrote a correspondent to *The Times*, "able and willing to go forth to minister to the sick and suffering soldiers of the East in the hospitals of Scutari? Are none of the daughters of England, at this extreme hour of need, ready for such a work of mercy?"

Florence was thirty-four years of age. Without hesitation she offered her services to the Government. They were accepted, and together with thirty-eight other nurses, whom she herself had selected, mainly from religious institutions, she set off for Constantinople. She promised her colleagues nothing but hard work. "The strongest will be wanted at the wash-tub," she told them grimly.

The party arrived at Scutari just after the battle of Balaclava, and went straight to the large barrack-hospital. Florence found that the reports of conditions, far from being exaggerated, completely understated the true situation. The hospital was overcrowded, understaffed, filthy, unventilated, and infested with vermin. There was hardly any medical equipment, few drugs and dressings, no clean clothing, little food, and an acute shortage of such essentials as soap and cleaning-material. The hospital was built to take a maximum of 1000 patients. The nurses found over 4000 already in, with others pouring in daily.

The arrival of Florence Nightingale had an immediate effect. The mere presence of the "Lady with the Lamp," as she came to be known, acted like a tonic on the unhappy soldiers, and by her kindness and gentleness alone she saved innumerable lives.

But she was not always kind, and could be anything but gentle. She might be the symbol of peace in the hospital wards, but in her office she was a determined and fearless fighter. She fought the hospital authorities, the doctors, the contractors, the Government officials—even the War Office itself! She asked and gave no quarter, never spared her words, and was ruthless with every one who did not conform to her high standards of efficiency. Her capacity for work was amazing, and she thought nothing of being on her feet for twenty hours a day. The extent of her achievement is best shown by simple statistics: in four months the hospital mortality was reduced from 42 per cent. to 2·2 per cent.

Florence remained at her post after the armistice, returning to England in August 1856. She was rightly treated as a national heroine, honoured by the Queen, and given an enthusiastic welcome by the whole population. Longfellow wrote a poem about her. A fund was set up to commemorate her work, and with it she founded the Nightingale School of Nursing at St Thomas's Hospital, London.

Florence Nightingale had accomplished two great tasks. She had saved the lives of countless soldiers, and she had raised the status of nursing to that of an honourable profession. Sairey Gamp had gone for good. Nurses were no longer regarded as inferior servants; other schools were set up, and the profession soon began to attract women with higher ideals.

Florence might have retired then, but she had a third task in mind. This was no less than the reform of the entire medical services of the Army. The war was over, but Britain still had a Regular Army. Peacetime barrack conditions were anything but healthy, and to the improvement of these Florence Nightingale devoted the rest of her life. She fought many battles with authority, and wrote innumerable pamphlets on the subject. The best known of her works was her *Notes on Nursing: what it is, and what it is not*. In 1902 the Queen Alexandra's Imperial Military Nursing Service, or Q.A.I.M.N.S., was founded, and the red cape which is still worn by its members was modelled

on the uniform designed by Florence for her gallant team of thirty-eight nurses.

In 1907 Florence Nightingale had the honour to be the first woman to receive the Order of Merit. This heroine passed away three years later, at the age of ninety.

R.A.M.C.

In the middle of the Crimean War a Royal Warrant was issued authorizing the formation of a "Medical Staff Corps." The scheme was limited, its chief defect being that no provision was made for the inclusion of medical officers. However, the idea was persevered with, and after the War the corps was replaced by the "Army Hospital Corps." This body was better organized, non-commissioned officers were included in the establishment, and special training was introduced. Doctors were still not included, the officers of the corps being non-medical men drawn from other regiments.

As the latter half of the nineteenth century was a period of practically undisturbed peace, military medicine was not considered very important. Thus little progress was made in the next twenty-five years, with the exception of a provision made in 1873 for the corps to have its own officers. The old name of "Medical Staff Corps" was restored, and certain minor reforms were introduced. However, the officers were still non-medical men, and it was not until eleven years later that authority was granted for the corps to be officered by doctors.

Then, on June 23, 1898, a new Royal Warrant announced the birth of the Royal Army Medical Corps. It was given the same status as the other corps and regiments in the British Army, and adopted as its badge the serpent of Æsculapius, with the motto *In Arduis Fidelis*. The new corps was soon to have its baptism of fire. Shortly after the beginning of the troublous twentieth century the Boer War broke out, and in this the R.A.M.C. gained a reputation that it has lived up to ever since. Six V.C.'s were awarded to members of the corps during that War, and the number of lives it saved cannot be computed.

A much severer test came in the War of 1914–18. The corps took the field with a strength of only 9000, which was eventually expanded to over 130,000. Nearly 7000 of these "unsung heroes of the battlefield" sacrificed their lives to save those of their comrades.

After 1918 the establishment was greatly reduced, but the standard of the corps never suffered. In 1939 the Army had at least one well-trained and organized service, and during the following six years the Medical Corps was represented wherever troops were stationed. No operation was undertaken without adequate medical staff and supplies. The normal training-programme was supplemented by instruction in such duties as airborne operations and Commando raids, and the R.A.M.C. had their red berets and green berets. Doctors and orderlies were even taught to ski in order to take their place with the troops engaged on the hazards of mountain warfare.

Administration

The R.A.M.C. has four main functions: the preservation of health, the prevention of disease, the collection and care of the sick and wounded, and the provision of medical supplies. Disease, and especially epidemic disease, has always proved more deadly to troops that the armament of the enemy, and in no sphere is preventive medicine more necessary than in the Army. Thus the R.A.M.C. is equipped with special Field Hygiene Sections, Sanitary Squads, Anti-Malarial Units, and Mobile Laboratories. After the 1914–18 War two new directorates were set up at the War Office—for Hygiene and Pathology respectively.

The head of the R.A.M.C. is the Director-General of Medical Services, better known as the D.G.M.S. He is represented in each theatre of operations by a Director of Medical Services, or D.M.S., who is in turn served by Deputy and Assistant Directors. The Directors of Hygiene and Pathology are represented in a similar way. Also under the immediate command of the D.G.M.S. come the Q.A.I.M.N.S., headed by a Matron-in-Chief, and the Army Dental Corps.

One of the most famous Directors-General was Sir William Boog Leishman, who made important contributions to the studies of tropical disease and anti-typhoid inoculation. He solved the problem that Ross had been set in the middle of his malarial researches—the cause of kala-azar; and the disease is now known as generalized leishmaniasis.

Evacuation of Casualties

The evacuation of casualties from the battlefield has been brought to a fine art, and great credit is due to the R.A.M.C. for the way it has adapted its system to meet the changing military tactics. The corps is now highly mobile, and each unit is trained to be prepared for swift advances and retreats at the shortest notice.

Every soldier going into action is issued with a 'first field dressing,' a small cloth-covered package which fits into a special pocket in the front of his battledress trousers. Inside this package are two sterile dressings in waterproof covers, each consisting of a gauze pad stitched to a bandage together with a safety-pin. Every soldier is trained in the use of this dressing, which often constitutes his first medical treatment in the field. Casualties that can walk make their own way back to the first medical unit—the Regimental Aid Post, or R.A.P. The more severely wounded are borne on stretchers by regimental bearers.

At the R.A.P. is the Regimental Medical Officer, who gives the bare minimum of treatment. Fractures are splinted, hæmorrhages stopped, dressings applied; morphia is injected to relieve pain, and emergency treatment is given for shock. All but minor casualties are evacuated as quickly as possible to the Advanced Dressing Station, or A.D.S., which serves several R.A.P.'s, communication being by both stretcher-bearers and ambulance. At the A.D.S., which is staffed by a section of a Field Ambulance, further emergency treatment is given, and the casualties are sorted, usually in the ambulances in which they arrive. Cases requiring further treatment for shock or immediate blood transfusion are normally sent straight on to

the near-by Field Dressing Station, to which a special Blood Transfusion Unit is attached. Others, requiring immediate operation, are despatched to the Advanced Surgical Centre, a sort of 'portable' operating-theatre, staffed by a mobile team including a surgeon and an anæsthetist. Finally, cases requiring neither of these types of immediate treatment are evacuated to the first large medical unit—the Casualty Clearing Station. This is a miniature hospital, with wards, theatre, and general-hospital equipment.

All serious cases, when fit to be moved, are transferred back to a General Hospital, the largest unit in the R.A.M.C. Further sorting takes place here. Some patients require treatment of a highly specialized nature, and are transferred to centres established at various base hospitals—orthopædic, maxillo-facial, neurological, etc. Finally, from the General Hospital the patient may either go to a Convalescent Depot or be discharged back to his unit or base depot as fit for duty. Seriously wounded cases, however, are generally evacuated to the United Kingdom.

There are four main types of medical transport: road ambulances, hospital trains, hospital ships, and specially equipped aircraft. Wherever possible General Hospitals are situated on railway lines.

Officers and Men

The duties of a medical officer are a good deal more varied than those of a civilian doctor. Considerably more than professional skill is required of him. He must have the additional qualities of leadership, personal courage, resourcefulness, presence of mind, and administrative ability. He is often called upon to make quick decisions, and he must always be ready to improvise in emergencies.

Not all the officers of the modern R.A.M.C. are doctors. The corps has its own quartermasters, men who have worked their way up from the ranks. The acute shortage of doctors during the 1939–45 War led to the appointment of quartermasters as registrars of military hospitals. These important

posts had formerly been held only by medical officers. Another innovation, which came comparatively late in the War, was the commissioning of 'stretcher-bearer officers'—non-medical men who began with the rank of 2nd lieutenant and who relieved doctors in minor administrative posts as well as in the evacuation of casualties from the battlefield.

The 'other ranks' of the R.A.M.C. are among the most highly trained soldiers in the whole of the British Army. The basic corps trade is, of course, that of nursing orderly; and every man, from the sergeant-major to the company runner, is expected to know something about nursing and first aid. The essential qualifications of a good nurse are defined in the official R.A.M.C. Training Manual as "cheerfulness, quickness, gentleness, tact, firmness, reliability, good powers of observation, cleanliness, thoughtfulness, patience, and loyalty"—a very high standard indeed!

As the R.A.M.C. is a self-contained corps there are numerous other trades as well as that of nursing. Medical officers' prescriptions are made up by fully qualified dispensers, who usually carry the rank of sergeant. Pathologists have a staff of trained laboratory assistants, while a hospital X-ray department has one or more radiographer to assist the radiologist. Hospital cooks prepare the special diets required by patients; clerks are responsible for notification of casualties and compilation of vital medical statistics. There are special sanitary assistants, masseurs, mental nursing orderlies, and many others.

In peace as in war, one branch of the British Army is never idle—the Royal Army Medical Corps.

The Navy and the R.A.F.

The medical services of the Royal Navy and Royal Air Force so closely resemble the R.A.M.C. that any detailed description would be largely repetitive. The Naval system is somewhat different owing to the special conditions prevailing on board ship; mention will be made in the next chapter of the work in this connexion of two famous naval physicians.

One of the pleasant features of the unpleasant 1939–45 War

was the degree of co-operation among the three medical services. Concessions were made on all sides to adjust differences in administration and organization, and almost without exception all ranks of the three services worked in the closest harmony.

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IN OUR TIME

NO historian can interpret his own age. Little things seem big at the time, while the really important matters are often overlooked. The survey that follows, therefore, does not pretend to be comprehensive, since it has had to be based on contemporary valuation, and that is notoriously unreliable. A medical historian of the eighteenth century devoted a whole chapter of his book to mesmerism, and dismissed the discovery of percussion in a single sentence. History rectified the error; and only history will be able to place the achievements of the twentieth century in their true perspective.

In every branch of medicine progress has been made. The most conspicuous advances have been in treatment, both medical and surgical. The former will be dealt with at some length in this chapter and the next, and a few words must be said here about modern surgical technique. Orthopædic surgery, which is the specialized study of bones and joints, was tremendously improved by the introduction of plaster-of-paris splints, applied direct to the skin, for the fixation of fractures. Meanwhile general surgery was being steadily expanded by the exploration of the old 'forbidden territories'—the skull, abdomen, and thorax. Bullets and tumours were removed from the brain. Part of the stomach was cut out, and the digestive system short-circuited. The spleen, either of the kidneys, and even a whole lung can now be removed with comparative safety. Even more dramatic, however, are the operations that have been performed on the organ that was for so long regarded as untouchable—the heart. When the heart has stopped beating, its action has been restored by massage by the surgeon's hand; when it has been wounded, stitches have been put in; and, most wonderful of all,

when its own blood-supply has flagged, it has been given fresh nourishment by a graft of muscles taken from the chest.

The Conquest of Yellow Fever

After malaria the most notorious disease peculiar to the tropics is yellow fever. It is less widespread, but far more virulent. In the epidemic in Rio in 1898 the death-rate reached the amazing figure of 94·5 per cent., while for many years the disease claimed two out of every ten British soldiers sent to Jamaica or the Bermudas. It was the slave-trade that carried the disease to South America and the West Indies from its native West Africa.

Like malaria, yellow fever was for long thought to be caused by some poison in the air; like malaria, its prevalence near marshes was observed. Similar suggestions of a connexion with mosquitoes were put forward. It was not until Ross's discoveries were made known, however, that a serious scientific investigation was begun. In 1900 the Americans set up a Medical Commission headed by Walter Reed, a U.S. Army doctor, which went to Havana to study the problem on the spot.

There was one sure way of establishing whether or not the disease was carried by mosquitoes. It was a very drastic way, consisting of the deliberate exposure to infection of human beings. The commission did not look for volunteers. Two of the members, James Carroll and Jesse Lazear, took it upon themselves to be the subjects for experiment. Mosquitoes were encouraged to feed on the blood of patients suffering from yellow fever—and then invited to bite the two courageous doctors. Both contracted yellow fever. Carroll lived to see the results of the experiment, but Lazear succumbed after a few days.

By this heroic sacrifice it was shown that mosquitoes were carriers. It did not prove, however, that this was the only means of infection. There was a current belief that the disease could be caught from contact with clothing, bedding, and other such articles. Another heroic experiment was made, this time by Dr R. P. Cooke and two volunteers from the U.S. Army

Hospital Corps. Soiled bedding was obtained from a local hospital, and the three volunteers spent twenty long nights between sheets and blankets that had every chance of causing their death. Happily the experiment had no such effects; and thus the mosquito was shown to be the only carrier of yellow fever.

As in malaria, it was a particular species of mosquito that was responsible. The guilt was tracked down to the stegomyia, and again it was the female of the species that carried out the deadly work.

Preventive measures were taken at once, and the Americans showed a speed and thoroughness in striking contrast with the dilatory methods that had so angered Sir Ronald Ross. Under the direction of the chief sanitary officer, W. C. Gorgas, Havana was purged of yellow fever in an amazingly short time. All existing cases were isolated in mosquito-proof buildings, and the insects themselves were attacked by drainage, spraying, and every other known method. The figures that follow speak for themselves. Up to the end of the nineteenth century Havana had an average yellow-fever mortality of several hundreds a year. The figure for 1900 was 310. Reed's report was published at the beginning of 1901; Gorgas began at once, and by the end of the year only eighteen deaths had occurred. In the next three years the figure was unchanged: nil.

By that time Gorgas had left Havana for Panama, where the stegomyia mosquito was helped in her evil work by the anopheles. The achievement of Gorgas and the subsequent construction of the canal have already been recorded.

Yellow fever was to claim another martyr to the cause of science. This was Hideyo Nogouchi, a Japanese investigator, who contracted yellow fever and died in West Africa in 1928, after a long but unsuccessful search for the cause of the disease. In the year of his death Sir Adrian Stokes, with his colleagues Bauer and Hudson, finally proved that the cause was not a spirochæte, as Nogouchi had believed almost to his death, but a virus. Three years later the laboratories of the Rockefeller Foundation produced the yellow-fever vaccine.

Vitamins

In 1740 Lord Anson took six ships of the Royal Navy on a voyage round the world. The voyage lasted four years, in the course of which no less than three-quarters of the ships' crews died of scurvy, the terrible disease characterized by swellings on the body, bleeding from the gums, and the falling-out of teeth. Scurvy was very common in both service and merchant ships, and it took a heavy toll of sailors until two naval doctors discovered not the cause but the correct means of prevention. The first of these, James Lind, wrote a book on the disease in 1753, in which he advocated a diet of green vegetables, fresh fruit, and lemon-juice. Twenty-five years later Captain Cook followed this advice with great success in his famous voyage of discovery. It was not until 1796, however, that these vital foods were placed on the official ration scale by another naval doctor, Sir Gilbert Blain.

In 1945 British troops returned from over three years' incarceration in prisoner-of-war camps in the Far East. Of the tropical diseases they had suffered the commonest were malaria and beri-beri. For those who were suffering from the second of these a diet including yeast and wholemeal bread was prescribed.

Neither scurvy nor beri-beri is caused by a germ. Both are diseases of deficiency, caused by a lack of certain qualities in diet. These qualities are called vitamins, and their discovery altered doctors' whole conception of the nature of foodstuffs. Dietetics had for long been a matter of balancing proteins, carbohydrates, and fats, on the one hand, and calories, or units of heat, on the other. Now a third factor was discovered, and medical science had a new course to follow.

The various vitamins are present in small quantities in a number of natural foodstuffs, but are largely destroyed by cooking and canning. They are also lost in processes designed to make food more palatable, such as the 'refining' of bread and the polishing of rice—the cause of so much beri-beri, which is due to a deficiency of the vitamin known as B 1. Scurvy is caused by a lack of Vitamin C, while the children's disease of

rickets is due to a deficiency of Vitamin D. This last is found in only a few foodstuffs, notably cod and halibut liver oils, sardines, and, to a lesser extent, milk, butter, and the yolk of eggs. The first of these has been advertised as 'bottled sunshine,' which is precisely what it is. For vitamins we now know to proceed from the ultra-violet rays of the sun.

The value of sunshine to health was known before vitamins. Towards the end of the nineteenth century Dr T. A. Palm, of Edinburgh, during a tour of duty in Japan, remarked on the freedom from rickets of children living in sunny countries, even when their diet was quite inadequate by western standards. In 1890 he wrote a paper advancing the theory that sunshine was fatal to rickets. After the 1914-18 War his theory was borne out by Dr Harriette Chick, of the London Pasteur Institute, and Dr Pirquet of Vienna. The children of Vienna suffered terribly at that time, and the supplies of foods rich in vitamins that were rushed to the city were insufficient for the population. Dr Chick, who headed a medical mission there, co-operated with Dr Pirquet, and they turned the lack of supplies to scientific advantage. Dr Pirquet took fifty babies from poor homes, put them in a children's hospital, and gave them plenty of fresh air and sunshine and a healthy diet—but little milk and no cod-liver oil. At the same time Dr Chick took another fifty babies and nourished them on these two foods. To the surprise of both doctors the two forms of treatment had the same result. Then winter came, and Dr Pirquet's babies began ailing again. Rickets broke out, and Dr Chick introduced the treatment of artificial sunlight. The babies recovered, and the source of vitamins was established.

Later, it was discovered that certain foodstuffs which contained no vitamins, such as margarine, could be 'charged' by a similar application of ultra-violet rays.

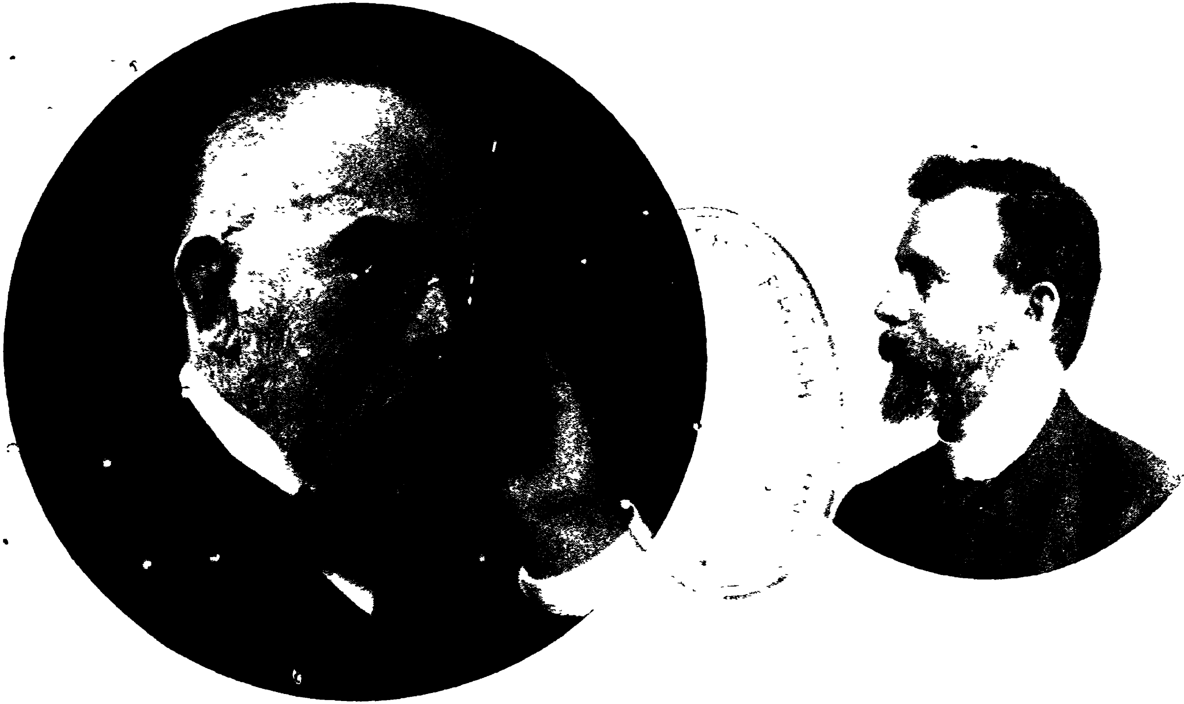
The Discovery of Insulin

"What sin has Pavy committed," asked Sir William Gull, "or his fathers before him, that he should be condemned to spend his life seeking the cure of an incurable disease?"

AN EMERGENCY OPERATION IN A DUG-OUT

Deep in the jungle of Bougainville, in the South-west Pacific, this dug-out was about four feet below the surface and roofed with heavy logs.

Photo Paul Popper



ROBERT KOCH, PIONEER IN BACTERIOLOGY — PAUL EHRLICH, HIS GREATEST PUPIL

Reproduced from History of Bacteriology ...

Frederick Pavy was a doctor of the nineteenth century. The "incurable disease" he was seeking to cure was diabetes.

In the twentieth century Frederick Pavy was vindicated.

The discovery of insulin was one of the greatest romances of twentieth-century medicine. It made life bearable again for sufferers from the 'hopeless' disease of diabetes, which still defied successful treatment after so many other diseases had been conquered.

The chief signs and symptoms of diabetes are loss of weight, intense thirst, and the presence of sugar in the urine. This sugar is one of the substances built up by the body from the food we eat. It is normally distributed to the tissues through the blood; in diabetes the content of blood-sugar, as it is called, is abnormally raised and overflows through the kidneys into the urine.

Blood-sugar is built up for the purpose of supplying the body with heat, energy, and nourishment. When it is thrown off as a waste product, therefore, it means that the body has lost the power to assimilate it. It is still being manufactured, but no longer being converted into the form the body needs. The blood is thus grossly overloaded with sugar while the tissues are starved from lack of it. Before insulin was discovered the only treatment consisted of reduction of the level of blood-sugar by the elimination of starchy foods from the diet. This was unsuccessful because it was the treatment of a symptom and not of the disease.

Now Claude Bernard had discovered that the digestion of food was accomplished mainly by the large gland known as the pancreas, or sweetbread. Later research traced the cause of diabetes to a defect in function of this organ, and the pancreas became the subject of close study. The process whereby the sugar was converted into the necessary form was eventually tracked down to collections of small cells in the gland, named the 'Islets of Langerhans,' after their discoverer. In these cells was the key to the problem of diabetes. They secreted the magic elixir which made the sugar fit for the body to absorb, and it was the reduction of this secretion that caused diabetes. If the body, therefore, could be supplied with this elixir in some other

form, diabetes might yet be conquered. Numerous extracts were made from the sweetbreads of animals, but their effect in treatment was nil.

The man who solved the problem was a Canadian named Frederick Banting. Born in 1890, he was still a student at Toronto University when war broke out in 1914. He volunteered for service with the Canadian Army and fought in France, where he was seriously wounded and finally discharged from the service as an invalid. Back in Canada he returned to his medical studies, obtained his degree, and set up in general practice. He was not very successful in this, and at first he had more spare time than he wanted. But already the disease of diabetes had aroused his interest, and he began to study it in his own little surgery.

In his observations on the pancreas Banting was struck by the tremendous power of the juices secreted by that gland. They could break up and dissolve all sorts of foods in the stomach, including the toughest of meats. It occurred to him then that their power might not be confined to the process of digestion, and thus he found out why the extracts that had been made from animals' sweetbreads had been non-effective. The pancreatic juices go on working after death—no longer in the useful process of digestion, but in destroying the very cells which have secreted them throughout life. The Islets of Langerhans are destroyed with the rest, and their precious elixir is lost.

No longer did Banting worry about the fortunes of his practice. Small as it was, it was too large for him to be able to devote enough time to the study that had become an obsession. Besides, he needed proper equipment and facilities for research. With the splendid impatience of youth he gave up his house, sold his furniture, and set off for Toronto. Henceforth he was going to be a scientist.

Banting was more fortunate than most pioneers. Instead of turning him away the authorities at the university showed a genuine interest in his work, and gave him practical assistance in the form of a small laboratory and a small salary. He was also given one assistant. Two of the medical students applied

for this post, and they settled their claims by the spin of a coin. The toss was won by Charles Best, whose work with Banting gained him a secure place in medical history.

It must not be imagined that Banting was working in the dark. The year before he went to Toronto he had read an article in a scientific journal pointing out that if the pancreatic duct, which carried the digestive juice from the pancreas to the small intestine, were ligated, then the cells producing the digestive juice would atrophy. Banting read this article one evening before he went to bed. At two o'clock the following morning he scribbled on a pad on his bedside table: "Ligate pancreatic duct of dogs. Wait six or eight weeks for degeneration. Remove the residue and extract."

At Toronto Banting put his idea to the test. Using chloroform as an anæsthetic, he ligated the pancreatic ducts in some of the dogs placed at his disposal. After waiting a few weeks he examined two of the animals, and found that his ligatures were ineffective, so that he had to begin again. The second time he was successful. After waiting another month he removed the pancreas of each dog, again under chloroform. In each case, he found, the pancreas had shrunk to about one-third of its former size; and the cells that produced the digestive juice were no longer active. From the pancreas Banting prepared a solution in saline, and injected it into a dog suffering from diabetes. The effect was like magic. The symptoms of the disease disappeared, and the dog's blood cleared of its excess of sugar.

That was the experiment that led to the discovery of insulin. In another experiment Banting obtained the insulin from the pancreas of a new-born calf that had not yet tasted food; for Nature, ever practical, does not provide the digestive juices until they are actually needed. Later, less expensive methods of extracting insulin were found, and its production in large quantities was carried out very largely under the direction of Best.

Before Banting tried his extract on human beings he and Best gave each other injections, to make sure it was not toxic to humans. Then he treated three diabetic patients. The

effect was the same as with the dogs. The patients responded as if the Islets of Langerhans were working normally again.

They were not, of course. The insulin, as it was called, was doing their work for them. Once the effect of the injection had worn off, all the old symptoms came back. For insulin does not effect a permanent cure, nor has any such cure for diabetes yet been found. The sufferer usually has to take insulin for the rest of his life.

But he owes his life to Banting.

The discovery was announced in 1922. Banting was only thirty-one, and the world was thrilled by his achievement. He was awarded the Nobel Prize for Medicine, and of the £7000 that went with the award he donated £2000 to further medical research. He died in 1941, mourned by the innumerable sufferers from diabetes to whom he had given a new lease of life.

Plastic Surgery

The plastic surgeon must be an artist as well as a scientist. His work is to repair deformities, to remedy natural defects, to beautify; thus this branch of medicine is sometimes, and perhaps more happily, known as 'æsthetic surgery.'

The first plastic surgeons were the ancient Hindus. The Ayur-Veda records the operation of rhinoplasty, or reconstruction of a destroyed nose. The Hindus performed this difficult operation by cutting a strip of skin out of the forehead, twisting it into the required shape, and 'grafting' it on to the stump of the missing nose. The other end of the skin-flap was left attached to the forehead until the new nose was growing, and then cut away completely and trimmed up. For a pattern the Hindu surgeons used the leaf of a tree.

Both the Greeks and the Romans performed a similar operation, and Galen extended it to the restoration of destroyed ears and lips. After this plastic surgery apparently fell into disuse until the Middle Ages, when the barber-surgeons made the first attempt to remedy the congenital deformity of harelip.

The first known specialist in plastic surgery was Gaspare Tagliacozzi, who held the Chair of Anatomy at Bologna for

thirty years. He repeated the Hindu operation of rhinoplasty, but used the skin of the arm instead of the forehead. Otherwise the procedure was the same, the limb being bandaged to the nose until the graft was completed. According to the poet Samuel Butler, Professor Tagliacozzi prepared noses from other sources, notably the backside of a porter:

> So learned Taliacotius from
> The brawny part of the Porter's bum
> Cut supplemental noses, which
> Would last as long as the Parent Breech—

but no longer, apparently. Butler narrated that this method was quite successful until the porter died, when "off dropped the sympathetic snout." It would seem that considerable allowance must be made to Butler for poetic licence.

In the next two centuries plastic surgery made little progress. This was not surprising; neither anæsthetics nor antiseptics had yet found their way to the operating-theatre, and the pain and danger of surgery did not encourage people to submit to cosmetic operations. Even in the latter half of the nineteenth century, however, progress was still very slight. Plastic surgery laboured under something of a stigma. To undergo a surgical operation merely to look more beautiful was regarded as extreme vanity, and sensitive persons preferred to put up with deformities rather than attract public cynosure and censure by having them remedied. If a person was born with a harelip, for example, he was expected to put up with it for the whole of his life rather than 'tamper with Nature.'

This attitude was not materially changed until the War of 1914–18. Then thousands of soldiers came home from the battlefields scarred and mutilated, and the distress and mental suffering of these heroes and their families made plastic surgery a necessity. Great work was done, and the results encouraged surgeons to pursue this branch of their profession in times of peace. By now public opinion was beginning to change, and it was no longer considered shameful for anyone to want to improve his or her physical appearance. Scars from accidental

injuries, burns, and congenital deformities alike were treated with increasing success, and plastic surgery emerged as one of the great medical achievements of this century.

Rhinoplasty was revived, in a very different form. Reconstruction of a completely destroyed nose was achieved by successive grafts of skin, mucous membrane, and bone or cartilage. Crooked noses were straightened, harelips corrected, eyebrows restored, scars, moles, and other facial blemishes removed. Nor was plastic surgery confined to the face. The scientific cult of beauty embraced the whole human body, and the correction of such distressing complaints as knock-knees and bow-legs was achieved.

The Medicine of the Mind

One of the worst evils of the Middle Ages was the treatment of sufferers from diseases of the mind. All mental disorders were grouped under the general term 'madness,' which was regarded as a sign of evil rather than of disease. The madman, therefore, was treated like a criminal. He was locked up in a special prison, under conditions rather worse than those in ordinary gaols (which were bad enough), and committed to spend the rest of his days in an iron collar and chains in a filthy, rat-infested cellar or dungeon. The only 'treatment' consisted of floggings and torture administered by the prison-keepers, who seem to have been specially selected for their exceptional brutality. Doctors did not normally go near such places, any organic disease being treated by visiting apothecaries. The notorious 'Bedlam' was a show-place for the curious, who paid twopence a head for the privilege of seeing the suffering inmates.

Not till the end of the eighteenth century was there any change in this outlook. Then the first move came not from the medical profession but from the Society of Friends, or Quakers. One of their number, William Tuke, founded the 'Retreat' at York, where condemned 'lunatics' were enabled to live in totally different conditions. Chains and iron collars were abolished, the sufferers were given decent food and accommo-

dation, and they were humoured and treated with kindness by the attendants.

Tuke's work was largely ignored by doctors, who still did not consider that mental disorders came within the scope of their profession. In the Golden Age, however, this view was radically changed. It was realized that humane treatment, although a vast improvement, was not enough. 'Madness' was a false generalization. There was a variety of different diseases of the mind, which required observation, diagnosis, and treatment just as much as the diseases of the body. A new specialty of medicine came into being—psychiatry, from the Greek 'psyche.'

The early attempts at rational treatment suffered because so little was known about the workings of the mind compared with those of the body. Then the whole study was revolutionized by the discoveries and theories of Sigmund Freud, a Viennese Jew. Born in 1856, he studied under Charcot in Paris, and his early work was based mainly on hypnosis. He eventually discarded this in favour of the method of 'free association,' and this led to the foundation of what is known as psycho-analysis. Freud discovered that the mind did not begin and end with consciousness; it had also a hidden part, which he termed the "unconscious mind," and which was capable of enforcing its wishes without their ever being consciously known. There was a constant conflict between the conscious and unconscious, which led to what he called repressions, to which most mental diseases could ultimately be traced.

From his study of abnormal psychology Freud was led to discoveries about the mind of the normal human being, and this he showed to be very different from the placid, controlled mechanism that it had formerly been considered. He applied his theories to give the first scientific interpretation of dreams, and he advanced reasons for such simple human actions as forgetting, losing things, laughing, and even slips of the tongue and the pen. His explanations were never very palatable, and the unconscious mind was shown to be full of what are generally considered highly unpleasant motives.

No man in modern medicine met with such bitter opposition as Freud. Apart from the scepticism of the medical profession, which at first regarded him as something akin to a charlatan, he was violently attacked by large sections of the general public. This was due partly to the fact that his theories, if true, repudiated the doctrine of free will, but more especially to the tremendous emphasis he placed on the instinct of sex. Like James Simpson, he was attacked on moral more than on scientific grounds. Much of this opposition was based on the absurd idea that Freud was advocating immorality; and only when it was realized that he was a scientist, interested only in discovering facts, did the criticism take a more scientific turn. For some time a fierce battle was fought between slavish Freudians, who did as much harm to Freud as the Galenists did to Galen, and equally uncompromising opponents. The controversy continues to-day; but so far as the medical profession is concerned Freud's teachings are accepted as largely true in fundamentals if not in details. Psychiatry is still in its infancy, and it will be many years before Freud's rightful place in medical science can be assessed.

At the age of seventy Freud was awarded the Freedom of the City of Vienna. Twelve years later his works were banned by the Nazis, and he himself had to flee for his life. He continued his work in London, where he died in 1939.

Contemporary with Freud was Carl Jung, a Swiss, who founded the school of 'analytical psychology.' The psychologies of Freud and Jung had many common factors, and each borrowed freely from the theories of the other. They also had considerable differences of opinion, however, notably on the function of the unconscious mind and on the sex-instinct. Jung is best known for his classification of human beings into 'types,' most famous of which are the 'extrovert' and the 'introvert.'

Psychological research was further stimulated by one of Freud's pupils, Alfred Adler, who eventually broke away from his teacher and founded the school of 'individual psychology.' While accepting much of his teacher's theory, Adler maintained that Freud over-emphasized the role of the sex-instinct and

underrated the will to power. Adler's work has had a far-reaching effect on child-psychology and education.

Despite the numerous divergences among the teachings of Freud, Jung, and Adler, it is now generally agreed that all three made valuable contributions to man's knowledge of the workings of his mind. The influence of their work has extended far beyond medicine. It has revolutionized philosophy, and invaded sociology, politics, literature, and even art. Much of the terminology of psycho-analysis has passed into everyday parlance, and it even found a way into a speech by one of its most vicious enemies:

"These inferior people," runs the text, "because of their *inferiority complexes*, display all manner of barbaric treatment of others."

The "inferior people" were the Poles; the speaker was Adolf Hitler.

Blood-transfusion

The history of blood-transfusion dates from the seventeenth century, when William Harvey made the great discovery of the circulation. The first recorded case of transfusion was performed in 1654 by a Florentine named Francesco Folli, who transferred blood from one living animal to another. Very soon after the Royal Society in England took up the subject. Sir Christopher Wren, the famous architect, was one of the first investigators, and one of the earliest experiments in this country was recorded by Samuel Pepys:

> At the Pope's Head. Dr Croone told me that, at the meeting at Gresham College to-night, there was a pretty experiment of the blood of one dogg let out, till he died, into the body of another on one side, while all his own run out on the other side. The first died upon the place, and the other did very well, and likely to do well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but, as Dr Croone says, may, if it takes, be of mighty use to man's health, for the mending of bad blood by borrowing from a better body.

The date of the entry is November 14, 1666. In the following year Jean Denys of Montpellier made the first experiment on a human being. His subject was a boy of fifteen, who was given blood from a lamb. "He grows fat visibly," reported Denys afterwards, "and is a subject of amazement to all those that knew him and dealt with him."

Within a few months of Denys's experiment a similar operation was performed in England. This also was reported by Pepys. The subject was one Arthur Coga, "a poor and debauched man," who hired himself to the Royal Society for twenty shillings. The experiment was carried out by Richard Lower, a Cornish physician, who was responsible for important discoveries about the effect of respiration on the blood. The blood-donor was a sheep, and the transfusion was apparently successful. Pepys contrived to meet Coga a week later. The latter declared he was in much better health as a result of the operation, and he showed no signs of any ill-effects, although he was, as Pepys put it, "cracked a little in the head."

Later experiments, however, were not so successful. Transfusion from animals to humans was often followed by death, and attempts at transfusion from one human to another met with little better results. As no reason for this could be found the operation was soon abandoned, and it was not until the twentieth century that it was restored. This came about as a result of the discoveries of Landsteiner and Shattock, who showed that there were different constituents in the blood not only of different species but even among different human beings. Different types of blood were incompatible with one another, and this was the explanation for the unexpected deaths that had followed transfusions in the past.

The work was carried a good deal further by the investigations of Jansky in Scandinavia and Moss in America, both of whom classified human blood into four distinct groups. One of these later came to be known as the 'universal donor' group, because it could safely be given to all human beings, irrespective of their own blood-groups. Another, much smaller, group was the 'universal recipient'; blood of this group could receive

from any of the others, but could only be given to blood of its own group. The other two groups were incompatible with each other, both as donors and as recipients.

Both Jansky and Moss numbered the groups serially, from I to IV. Unfortunately they used different enumerations, so that the figure Jansky gave to the universal donor was Moss's symbol for the universal recipient, and *vice versa*. This led to considerable confusion and even tragedy. In an attempt to settle the matter an American Medical Committee ruled that Jansky's numbering should be generally adopted as it was the earlier. This only increased the confusion, however, for Moss's notation was already more widely known. Finally, the question was solved by an international code, which used letters instead of numbers, *viz.*, AB (universal recipient), A, B, and O (universal donor).

The greatest technical difficulty in blood-transfusion was the invariable clotting of blood outside the body. Various attempts were made to overcome this obstacle, the most important being the introduction of sodium citrate by Professor L. Agôte, of Buenos Aires, in 1914. Blood-transfusion in its new form was used in the 1914–18 War with great success, especially in the last two years.

Nowadays direct blood-transfusion is comparatively little employed. Science has found the means to preserve and store supplies of blood, and in 1935 the Emergency Transfusion Service came into being, with 'blood banks,' as they are called, set up all over the country. The blood bank has great advantages over the old direct-transfusion method. It provides a ready supply of blood for immediate use in emergency, and no time is wasted in 'grouping,' which is done before the blood is stored. Further, the danger of transmission of disease is excluded by laboratory tests.

The blood-bank system proved of enormous value in the War of 1939–45, in the treatment of both service and civilian casualties. Its efficacy was greatly increased by the discovery of a process whereby the plasma of the blood could be dried and stored in powder form. Dried blood plasma contains all

the properties required for resuscitation, and it has the added advantages of being readily portable and keeping for an almost indefinite period of time. Moreover, it is compatible with the blood of all four groups.

Blood-transfusion is still used mainly to replace blood lost after injury or operation, but it has also become part of the treatment for certain types of anæmia and other diseases.

16

MODERN MARVELS

IT has been seen that during the last century there was a healthy reaction against the indiscriminate use of drugs, and the scientific discoveries did much to assist this. Reasons had been found for so many things that doctors became chary of doing anything without a definite reason. The germ theory of disease, the antiseptic method, the principle of immunity—all these had been beautifully explained by their discoverers. Little was known about the action of internal drugs, however. The value of certain of these in the treatment of specific complaints—such as the use of cinchona for malaria—was established; but these were exceptions. In general, drugs were coming to be regarded as mere palliatives, alleviating the symptoms without curing the disease, or a much-overworked form of the psychological treatment of reassuring the patient that something was being done for him—a form of treatment to which patients cling just as tenaciously in modern times.

There was good reason for this scepticism. Most drugs were traditional in origin—and medical science had wrought havoc with the most cherished traditions. Thus it was that the profession as a whole inclined more and more to the views of Sir William Gull, while scientists devoted their labours to the more fruitful study of vaccines and anti-toxins, which were proving so effective in both prevention and cure.

Meanwhile pharmacology, the science that deals exclusively with drugs, was radically overhauled. The number of drugs was reduced, and an examination was begun of their precise constituents. Drugs then were mainly vegetable in origin, and it was realized that in many cases only part of the compound was effective in medical treatment. Attempts were made to isolate this part, to make a purer drug; and by this method

quinine had been extracted from cinchona, and another alkaloid, emetine, from the ipecacuanha used in the treatment of amœbic dysentery.

At the same time efforts were being made by some ardent workers to prepare new drugs with similarly specific action against other diseases caused by infection. Not satisfied with the vegetable drugs already in use, they turned to chemicals for their raw materials. And out of these researches was born the greatest advance of the twentieth century so far—the wonder of chemotherapy.

Chemotherapy

The word literally means 'treatment by chemicals.' Such treatment was not originated in the twentieth century, or in the nineteenth. Paracelsus, it will be remembered, looked to chemistry for many of his prescriptions; and compounds of mineral origin were used in medical treatment by the Egyptians and even Babylonians. But modern chemotherapy was based on more scientific principles—the principles discovered by Louis Pasteur and his followers. It was another phase in the war against germs.

The aim of the new campaign was to discover an internal antiseptic that would kill micro-organisms already in the body, just as Lord Lister had killed them by the external application of carbolic acid. Indeed, in 1873 an attempt was made to use this very agent to "disinfest the blood" by means of injections, The attempt failed, of course, nor was the reason far to seek. The one great drawback to the use of antiseptics, as Lord Lister discovered, was that any chemical that killed bacteria invariably had a similarly destructive effect on the body in which the bacteria were lodged. To be effective, therefore, any 'internal antiseptic' must be able to kill the enemy without seriously harming the body that had been invaded. What were needed, as Paul Ehrlich put it, were "magic bullets which strike only those objects for whose destruction they have been prepared."

Paul Ehrlich, a German-Jewish pupil of Robert Koch, spent

most of his life seeking these elusive "magic bullets," which he was convinced must exist. It was no easy search.

> It is easily possible [he wrote] to arrive at a very large number of substances which will destroy bacteria and allied substances in aqueous solutions. But, of course, the problem is much more difficult when it is a question of internal disinfestation or of the destruction of living parasites within the infected organism. If the problem is set before us of sterilizing a room, then indeed it is an easy matter to do so, owing to the present advancement of science; but the task becomes more difficult when the room is filled up with materials, and when the materials are of such a delicate sensitiveness as living cells then the difficulty of the problem will be manifest without any further explanation.

"606"

Ehrlich's researches began on the aniline dyes that are derived from coal-tar. He was very familiar with these dyes, for they were used extensively in the process of 'staining' the transparent bacteria so that they could be observed under the microscope. But the dyes had another potential use; they could, it was found, destroy some forms of bacteria. Ehrlich experimented with them on dogs, and succeeded in destroying parasites in their bodies without seriously harming the animals themselves. He himself did not succeed in producing a drug that was effective in treatment of human beings, but the value of this part of his work was revealed later. Others followed up his researches, and in 1920 came the discovery of the famous "Bayer 205," which has proved so valuable in the treatment of African trypanosomiasis, or 'sleeping sickness.'

In 1905, meanwhile, the cause of the dread disease of syphilis was traced by another German bacteriologist, Fritz Schaudinn, to a micro-organism which he called the *Spirochæta pallida*. Up till then this disease had generally been treated with mercury, which was difficult to apply and dangerous to the body. Ehrlich considered arsenic, a highly toxic chemical which had already been used in various forms to combat certain diseases of the blood. He sought a compound of arsenic that would

kill the spirochæte without causing serious harm to the body.

Ehrlich prepared no fewer than six hundred and five different compounds, all without success; then, in 1909, he finally achieved his ambition. He discovered "Salvarsan," or arsphenamine—or, more simply, "606." Innumerable experiments were made on animals, and in 1910 the drug was tried on a human being. It was successful. Further, it was found to be effective in the treatment of other diseases, including anthrax, Vincent's angina, yaws (frambœsia), and rat-bite fever.

"606" was not entirely free from harmful effects, however. Arsenical jaundice, dermatitis, and even blindness could be caused by it, and great caution was needed in its administration. Meanwhile Ehrlich continued his researches, and in 1912 introduced "914," or "Neosalvarsan." The ill-effects of this were less marked, although by no means negligible. It did not completely fulfil the exacting requirements of the "magic bullet"; but it represented a great advance in medical treatment, and its discovery served as an inspiration for later workers.

For his pioneer work, Paul Ehrlich may be considered the 'Father' of that young but virile offspring, Chemotherapy.

Synthetic Drugs

A few words must be said about the source of the drugs prepared by Ehrlich. They were not, as has been said, of vegetable origin, but were obtained by what is known as synthesis, or building up, from chemicals. This process has played a tremendous part in modern medical chemistry. It has not only given medicine wonderful new compounds such as "606," but has also made possible the preparation from inorganic matter of drugs normally obtained from vegetable substances.

There are two main disadvantages to extraction of drugs from vegetable sources. One is the obvious difficulty of the obtaining of sufficient supplies, and the other concerns the purification of the products obtained. Preparation by syn-

'M & B 693'

By courtesy of Pharmaceutical Specialities (Messrs May and Baker), Ltd, and the "Illustrated London News"

TESTING THE SULPHONAMIDES: SLIDE-CELL TECHNIQUE

thesis has gone a long way to overcome both these problems. The chemical formula of the drug is first ascertained—by no means an easy task—and then, instead of being extracted from a living plant, the preparation is compounded from chemicals in a laboratory.

One of the greatest triumphs of synthetic preparation occurred during the 1939–45 War. A large proportion of the world's supply of cinchona bark fell into the hands of the Japanese, and quinine, the only known specific against malaria, became more and more difficult to obtain. Synthetic substances were prepared, chief of which was mepacrine, which actually proved more effective in preventive treatment than quinine itself. Credit for the discovery of mepacrine cannot, however, be claimed by the Allies. The drug was first synthesized by German scientists, and introduced by them—under the name "Atebrin"—as long ago as 1930.

The Sulphonamides

Despite the undeniable value of Salvarsan, chemotherapy did not prosper in the next decades. No significant new discovery was announced; and medical scientists began to despair of ever attaining to Ehrlich's ambitious "*cribrum therapeuticum*," by which all forms of infectious disease would be conquered. Salvarsan and Neosalvarsan, for all their usefulness, had their limitations. Their power against certain diseases—especially those, like syphilis, caused by spirochætes—was undeniable; but although the arsphenamides were found to have an activity against a number of bacteria, their value in treatment was severely restricted by their toxicity.

Then came the discovery of the group of drugs known as the sulphonamides—so called on account of their content of sulphur and nitrogen. And whereas the credit for Salvarsan must go almost entirely to one man, the sulphonamides were prepared and brought to medical practice by a truly glorious international effort in the midst of an age of extreme nationalism.

In the early history of the suphonamides the accent was on chemistry rather than therapy. The story begins in Vienna,

where a chemist named Gelmo synthesized a compound with the formidable name of para-amino-benzene-sulphonamide. This was in 1908, and nobody at the time considered this preparation as a possible drug. Sulphonamide compounds, however, soon engaged the attention of industrial chemists, and they were quickly exploited for use in the textile industry, notably for the dyeing of wool.

Various other sulphonamide compounds were synthesized, culminating in the preparation in 1932 of what was called "Prontosil." By this time suggestions had been made about possible therapeutic uses for these chemicals, and in the following year Gerhard Domagk contributed a paper to a German medical journal in which he claimed that Prontosil had the power to prevent the growth of certain germs in living tissues. Domagk based his report on results obtained from experiments with mice and rabbits. He had injected lethal doses of two kinds of bacteria into the animals, and then administered Prontosil. In all cases the infections were combated, and some of the infections were completely overcome.

The two kinds of bacteria used by Domagk were staphylococci and streptococci. The former of these, which appear under the microscope like a bunch of grapes, are the germs of common infections like boils and abscesses. The latter, which resemble a string of beads, produce erysipelas and severe infections of wounds and of the blood-stream, including the majority of cases of infections after childbirth. Prontosil was found to be most effective against streptococci.

Prontosil was tried out in medical practice, and Domagk's claims were soon supported. The new drug was found to be amazingly powerful in the treatment of certain diseases, especially those caused by streptococcal infection. Meanwhile chemists were synthesizing new sulphonamide compounds, and already the work had been taken up in France, Britain, and the U.S.A. In 1935 a group of French workers discovered that Prontosil broke down in the tissues into two separate compounds, only one of which was effective against bacteria. This they synthesized, and in the following year reports from Britain

revealed that the simpler compound was much more effective than Prontosil. Americans and others confirmed these results, and in 1937 the Council on Pharmacy and Chemistry of the American Medical Association gave the compound the name of 'sulphanilamide.' Its formula has a familiar ring: it is none other than para-amino-benzene-sulphonamide, first synthesized by Gelmo in 1908!

"M & B 693"

Meanwhile research was being pursued more vigorously than ever. The principal investigations in England were being carried out in the famous Dagenham laboratories of Messrs May & Baker, where ambitious attempts were being made to synthesize a compound with a wider range of treatment than sulphanilamide. The immediate target was one of the commonest of all dangerous diseases—pneumonia. Numerous preparations were synthesized, culminating in a compound with the truly awe-inspiring name of 2(para-amino-benzene-sulphonamido) pyridine, or—not quite so long, but bad enough—2-sulphanilyl-aminopyridine. Nobody could be expected to use a name of this length, so the new drug was called 'sulphapyridine' for short. But the name under which it became world-famous was taken simply from the number in the register in which all new compounds were entered—693.

"M & B [May and Baker] 693" was first used on March 18, 1938, for the treatment of pneumonia in a Norfolk farm-labourer. The case had been practically given up as hopeless. Within a few weeks of the first administration of the drug the man was well on the way to recovery. (Incidentally, it may be added that this patient was not the first person to take "M & B 693"; the laboratory research workers had satisfied themselves of its low toxic effect by the simple means of trying the drug on themselves.) In June of the same year another successful case of pneumonia treated by sulphapyridine was reported in *The Lancet*. It was followed soon after by an analysis of a hundred cases treated in the same way, and the value of the drug was established. For the first time in medical history a specific

drug cure for pneumococcal infection had been discovered. But that was not all. "M & B 693" had been used in the treatment of other diseases, and striking success was reported, especially in cases of the common form of meningitis and of gonorrhœa.

In the pharmaceutical laboratories research work was still going ahead. Sulphapyridine was followed by sulphathiazole, which was considerably more active against staphylococcal infection, and less toxic than any of the former sulphonamide drugs. Then, in 1940, came sulphaguanidine, effective in bacillary dysentery and certain other intestinal infections. Sulphadiazine followed in the same year, and in 1941 sulphamethazine was added to the list. Others followed, and new compounds are still being prepared. The story of the sulphonamides is not yet complete.

To-day the original Prontosil is but rarely used. Sulphanilamide is still used in milder cases of streptococcal infection, but both this drug and the famous "M & B 693" have been largely superseded by sulphathiazole and sulphadiazine. Each of the sulphonamides is normally prepared in the form of tablets, which are crushed and administered orally in water or milk. The drugs can be given also by injection and in the form of powders, lotions, and ointments.

Mention has been made of the toxic effects of the sulphonamides. These have been largely reduced with each new preparation, but are still never completely absent. The common symptoms are nausea, vomiting, headaches, general depression, and malaise. Complications of a more serious nature sometimes occur, especially in the renal system, although this has been largely counteracted by the giving of alkalies and copious fluids.

The action of the sulphonamides cannot be truly described as antiseptic. They do not themselves kill germs, but attack them indirectly. By chemical action they interfere with the normal food-supply on which the bacteria depend, thus slowing down their growth and preventing multiplication. As a result of this the bacteria are in no fit state to fight an aggressive

action, and their actual destruction is safely left to the natural defences of the body.

The Wonder Drug

The story of penicillin begins in 1918. In that year a paper appeared in the *British Journal of Surgery* on the use of antiseptics in the treatment of wounds. It was based on practical experience of war surgery, and it made the point that most of the chemicals used for this purpose did more harm than good. Not only did they fail to kill all the bacteria present, but they wrought greater destruction among the leucocytes—the very cells in the blood designed by Nature to fight the germs.

This paper attracted little notice outside the profession. It was a simple statement of a problem that was gaining the increasing attention of surgeons. Asepsis was the ideal, and germs could be excluded in the operating-theatre—but how were they to be combated when they had already gained a strong hold on a wound received on the battlefield? The paper stated the matter clearly and concisely, but it offered no solution.

It was not until ten years later that the author of this paper discovered the drug that was eventually to lead to that solution.

His name was Alexander Fleming. He worked as a bacteriologist at St Mary's Hospital, London, and there it was that the marvel of penicillin was discovered. Numerous stories have been written about this discovery, but only one gives a really true picture of it. That, of course, is Professor Fleming's own report, on which the present account is largely based.

Those ten years were not spent idly. Professor Fleming studied the problem from every angle, and in the study of culture-plates his keen eyes detected the presence of a *natural* antiseptic, which he called "lysozyme." Lysozyme is a ferment which is found in human tissues, tears, and other sources. The word is not well known among the general public, because the substance was not found suitable for treatment of human beings; this discovery of Fleming's is important, however, as

complete disproof of the suggestions that the later discovery of penicillin was an 'accident.'

In 1928 Professor Fleming was carrying out a series of experiments on staphylococci. He used plates spread with a jelly-like material for feeding the microbes, and examined the results under the microscope. Now to do this he had to remove the covers from the plates—and that meant that the cultures were exposed to the air and therefore to contamination. So when he came to examine the plates, he was not surprised to find a greenish-blue mould growing on the edge of one of them.

The mould grew—and a startling thing occurred. The microbes round it began to disappear!

There seemed to be nothing peculiar about this particular mould. It was just the sort of fluffy mass that brings a groan from the housewife when it appears in her larder. Damp bread, cheese, and preserves are favourite breeding-grounds for this undesirable fungus. The genus is called *Penicillium*, which means 'brush-like,' descriptive of the microscopical appearance of the mould as it develops. It is interesting to note that some of its properties had been observed by Louis Pasteur in his early studies on crystallography.

Fleming immediately began to investigate the phenomenon. So far the mould had shown a powerful influence on staphylococci. Now he tested its effect on other forms of bacteria. These experiments were later described by the Professor, in the delightful detached way of the true scientist:

> One of the first experiments was to plant some spores on an agar plate and allow them to develop at room temperature . . . for four or five days, after which a variety of bacteria were streaked across the plate radially to the mould colony. It was found that some of them grew right up to the mould, but others were inhibited for a distance of an inch or more. This showed that the mould produced an anti-bacterial substance readily diffusible in agar, which acted only on certain bacteria. This is the simplest method of testing any stray mould which turns up on a culture plate. . . .

The jelly-like substance called agar, which is used among other things for the preparation of anti-typhoid vaccines, was to play a large part in the later development of penicillin. It is made from seaweed, and much of its collection from the coast of Devon and Cornwall was done by volunteer workers.

Fleming had now shown that penicillin, as he called it, had a powerful effect on other forms of bacteria as well as the staphylococci, but not on all. The next step was to isolate and produce the substance free of the mould. He did this by growing penicillin in a meat broth, on the surface of which it took the form of what he graphically described as "a feltish mass." The fluid was strained through a fine filter. Further tests were made, with the same favourable results.

A new *natural* antiseptic had been discovered.

Now came the crucial test. How would penicillin act on leucocytes? If it should destroy these as well as bacteria, then . . . but it did not. It had no toxic effects on leucocytes whatever—and yet in the destruction of bacteria it was something like three times as strong as carbolic acid. "It was this," said Professor Fleming, "that convinced me that some day it would come into its own as a therapeutic agent, and led me, in 1929, to suggest that it might be an efficient antiseptic for application to, or injection into, areas infected with penicillin-sensitive microbes."

That day had not yet arrived. Penicillin, in its crude form, was unstable. It was tried on a few patients in St Mary's Hospital, but the practical difficulties were great. "When we asked the surgeons if they had any septic cases they never had any, and then perhaps they asked us if we had any penicillin and our whole supply had become inert. . . . We were bacteriologists, not chemists, and in view of the difficulties the chemists have had in concentrating penicillin it is not surprising that our amateur efforts at concentration were not successful."

This did not mean that Professor Fleming had abandoned hope. He kept his original culture-plate, on which the mould was first observed, and it can be seen to this day—dried up,

but still recognizable—in a place of honour in the Museum of the Medical School of St Mary's Hospital.

From Theory to Practice

The scene changes from the laboratories of St Mary's Hospital to the London School of Hygiene and Tropical Medicine. There Professor Harold Raistrick tackled the problem of transforming this crude penicillin into a drug that could be used to combat infection. A suitable nutrient liquid was evolved on which the mould could be grown, and it was found that this liquid, from which the mould had taken its nourishment, contained after some days the penicillin which had been produced. This liquid, however, contained only a relatively small quantity of penicillin, and it was found that by acidifying this liquid the penicillin in it could be extracted with ether. But he was unable to obtain a more concentrated form of penicillin, and could get no further. The importance of Raistrick's researches was not appreciated, and lack of support and assistance constantly impeded his work. It had not yet been generally realized that a priceless treasure was hidden in that common mould.

It was not until 1938 that other workers took Professor Fleming's culture and Professor Raistrick's synthetic medium and commenced the investigations that were to bring a miraculous drug to the aid of suffering man. This work was carried out at Oxford, and no longer was it a case of individual investigators working with inadequate assistance. A team of brilliant scientists was assembled, headed by Professors Florey and Chain. It is significant that Professor Howard Florey had spent much of the previous decade on the preparation of lysozyme, the first 'natural antiseptic' discovered by Fleming.

In that decade a great change had come about in the realm of drugs. Chemotherapy no longer depended on the discoveries of Ehrlich for its reputation. The sulphonamides had already proved their worth, and vast strides had been made in the practical preparation of such drugs. At last it was possible to attempt the difficult task of producing effective penicillin.

The Oxford team was given a grant of £350 from the Rockefeller Foundation—small enough for their tremendous task, but a fine gesture all the same. As has been seen, most scientists count themselves lucky if their work is not actually obstructed. The immediate task before Florey and his colleagues was to obtain a concentrate of the drug. A full description of the means by which this was achieved would be too long, complicated, and technical for the present account; suffice it to say that a concentrate was obtained by extracting the acidified penicillin solution at a low temperature with ether—the method earlier attempted by Professor Raistrick. The product was a reddish-brown powder, very impure, and containing only about one per cent. penicillin.

That one per cent. worked wonders. It was hundreds of times more powerful than the original fluid, and could counteract lethal doses of streptococci and staphylococci injected into mice. It was especially effective against the latter organisms. Moreover, the Oxford workers were able to confirm Fleming's observation that the leucocytes were unharmed, and the way was clear for a test on human beings. Before this could be done, however, some means had to be found of increasing production. Although the concentrate could be safely diluted to a fraction of its strength, the cost and labour to obtain a tiny quantity of the powder made the existing method of extraction impracticable.

One of the team, Dr Norman Heatley, designed a plant, and after numerous difficulties and setbacks it was at last found possible to prepare enough of the powder to continue the experimental work on a more ambitious scale. So, in the autumn and winter of 1940–41, the first cases of human beings were treated with the new drug. Only cases that had failed to respond to other forms of treatment were chosen, and the treatment was strictly limited by the smallness of the available supply. Even so, the results more than justified the research workers' hopes. As with mice infected with staphylococci, the same organism infecting human beings was found to be exceptionally vulnerable, and once again there was a significant absence of all toxic effects such as were caused by the impurities in the preparation.

There could hardly have been a worse time for research of this nature. Britain was fighting alone, England was being subjected to the most determined air raids in history, and the whole of the nation's industrial resources had been mobilized for the war effort. Quite apart from the tremendous technical difficulties that had to be faced, these conditions made it impossible for any large-scale production to be attempted in England. At the same time, penicillin was never so necessary. If it could be manufactured now, countless lives of soldiers might be saved.

In the summer of 1941 Professor Florey set off for the U.S.A. He was accompanied by Dr Heatley, and the remainder of the Oxford workers carried on with their tests. Florey had only limited results to show, but the Americans responded with both appreciation and energy. Production was begun in the United States, and new research workers joined in the task of overcoming the difficulties of manufacture. One of the most striking advances made in the United States was the discovery that corn-steep liquor, when added to the nutrient liquid on which the penicillium was grown, increased the yield of penicillin. Corn-steep liquor is a by-product in the starch industry, formed at the stage when the maize is left to steep. The exact way in which this substance acts is still not clearly known, but it has certainly been the most effective of the commercially available substances for increasing the yield of penicillin.

Meanwhile, clinical experiments had been proceeding in England. In 1942 Professor Fleming used the new preparation, and he was so impressed by the results that he got in touch with the Minister of Supply. The result of this interview was that penicillin was virtually nationalized. The nation could not afford competition. A Penicillin Committee was set up by the British Government, and all resources, public and private, were pooled.

Working in close co-operation, the British and American manufacturers gradually overcame their tremendous difficulties. All through 1942 they laboured, but in the summer of 1943 the Eighth Army in Egypt had only enough penicillin to treat

fifteen men. Then, in June of the same year, the Americans placed all manufacture under the direction of the War Production Board. Within a matter of months the whole situation had changed.

The figures that follow are given in 'units,' and it will be as well to explain at this point exactly what the penicillin unit is. In the first place it must be understood that the reason why this drug was not measured by weight was that a pure preparation had not been manufactured. The unit of penicillin, then, was based on potency, and it was fixed as the smallest amount which, when mixed with 50 c.c. of broth, would just prevent the growth of a particular strain of staphylococcus. Put in another way, this is equivalent to about 0·6 of a millionth of a gram of pure crystalline sodium penicillin. This amount is, of course, very small indeed, and on the average some hundreds of thousands of units are required for the treatment of a single patient.

When the U.S. War Production Board took over penicillin only 400 million units had been manufactured in America altogether. In the same month this figure was doubled, and in July it was doubled again. Two months later the figure had shot up to five billion. In July of the following year the amazing figure of 130 billion units had been reached—and this was to be more than doubled later!

By comparison with the American figures the output in the United Kingdom was small. The average monthly production in this country in 1943 was 300 million units. In the following year it had jumped to 3166 million units, and in 1945 the average was up to 26,000 million units. They seem modest figures compared with the amounts produced by the superior resources of the U.S.A.—but America was never in the front line. The significance of the British figures is better understood when it is realized that by far the greater part of the penicillin produced in this country during the War was manufactured within the target of bombs, V1's, and V2's—in the famous Glaxo Laboratories at Greenford, Middlesex, which suffered twice from direct hits and still carried on.

The Manufacture of Penicillin

The greater part of penicillin which was manufactured in England during the War was produced in glass flasks. First a nutrient liquid was introduced into these flasks. Then the flasks were plugged with non-absorbent cotton wool, and the whole was carefully sterilized. ' Seeds ' of the Penicillium mould were introduced into each flask, and these were kept at a carefully controlled temperature for about eight days. After this time a pale blue-green 'mat' of the mould had developed on top of the liquid, and this mould was filtered off. The liquid remaining in the flask was then collected for concentration and purification of the penicillin it contained.

While this method of producing penicillin was the only possible way during the War, it had long been recognized both in England and in the United States that a single tank of large size could replace the innumerable small flasks, and it is this method—known as the 'deep culture' method of producing penicillin—that is now used exclusively. For this the requirements of the living mould are the same as in the small flasks. A supply of sterile air must be available, the temperature must be carefully controlled, and the liquid must contain suitable nutrients. Since the mould does not grow on top of the liquid, but throughout the liquid, the whole mixture is kept stirred. The tanks used for this process hold something like 5000 to 10,000 gallons, and there will be several of these so that the process is continuous. This method of manufacture has enabled penicillin to be produced in much larger quantities—and with greater purity.

The methods of purification and extraction are similar in this process to those used with the flask method, and involve the extraction of the penicillin from the aqueous culture liquid with suitable solvents after acidification. The method is too complicated to go into in any great detail, and it is sufficient to realize that in the repeated transfers from solvent to solvent a highly concentrated solution of penicillin is obtained. By a special method the amount of penicillin in this concentrate is

estimated, and from this estimate is worked out the quantity of penicillin solution which must be filled into the final container to give the required number of units. Using the highest standards of cleanliness to prevent contaminants from entering the active solution, the vials in which the penicillin is eventually to be sold are filled. The process of filling is a semi-mechanical one, and is operated by a worker clothed like a hospital surgeon.

The liquid in the vials has now to be dried, and this must be done without the temperature of the penicillin being raised. This is accomplished by a process known as freeze-drying, in which the water in the solution is first frozen to ice at a temperature many degrees below freezing-point, and is then evaporated in a nearly perfect vacuum, passing from ice to water-vapour without becoming a liquid at all. In practice the filled sterile vials are placed in stainless steel trays fitted with special covers of material similar to that used in gas-masks, through which no bacteria can enter; the trays are put in a refrigerator to freeze the contents of the vials, and then transferred to a special chamber where they are freeze-dried. The temperature is brought many degrees below the freezing-point of the penicillin solution in the vials. The air is exhausted from the chamber, and as soon as a sufficiently high vacuum has been reached, the ice from the frozen solution in the vial evaporates without melting and condenses on special coils. So cold does the vial contents become that it is necessary to apply heat in order that the temperature is not so far below freezing-point that evaporation cannot take place. Actually the effect obtained is like that of ice standing immediately over a large electric fire and yet not melting but disappearing—passing from the solid form into water-vapour. The apparatus for carrying out freeze-drying is rather complicated, but it is sufficient to know that the penicillin solution is freed from the moisture at an extremely low temperature, which cannot harm the active drug. The vials containing the light powdery penicillin are capped aseptically, and after labelling are ready for market.

To supplement this brief account of the manufacture of penicillin a few words must be said on the subject of impurities.

Perhaps the word 'impurities' is misleading. It is used from the point of view of the chemists, who rightly believe that anything that does not contain 100 per cent. of a chemical substance is impure, regardless of what the impurities may be. In the case of penicillin the most obvious of these impurities is the yellow colouring matter; but fortunately these impurities, in the amounts that are present in the commercial penicillin nowadays, are not harmful to the patient even when large doses of penicillin are given.

This is a different story from that of 1945, when much of the penicillin was only 30 per cent. pure, and large doses gave unpleasant reactions as a result of these impurities—so that the discomfort of the cure was sometimes as bad as that of the disease!

That was from the patient's viewpoint. From the chemical side the material containing large quantities of impurities did not keep well, but gradually lost potency. Nowadays the commercial penicillin, of 80 to 90 per cent. purity. will keep quite well in a cool, dry place.

In the course of research it was natural that the chemist should wish to obtain pure penicillin. At Barnard Castle it was found that the commercial material obtained from the mould could be further purified to give a white powder that was 100 per cent. penicillin. This purification gave relatively poor yields; that is, some penicillin was lost during its purification. While there was a world shortage, therefore, it was not wise to reduce the quantity for quality when for most purposes the 90 per cent. material was satisfactory.

Recently the sodium salt of penicillin was made available in *crystalline* form from which impurities were absent. This crystalline penicillin was found to have enhanced stability, withstanding higher temperatures, and for longer periods, than any other form of penicillin.

The purification of the penicillin made by the mould did not tell the chemists much about the chemical structure of penicillin, and obviously if the pure material could be made by building up from chemicals of known structure—that is, by

synthesis—it would assist in the understanding of how the drug worked and behaved. This synthesis has now been achieved; but the quantities obtained in this way are so small that the price would be prohibitive, and obviously purification of the penicillin obtained naturally is a better proposition. This synthesis did, however, achieve its object in adding to our knowledge of the structure of penicillin, and may yet be simplified enough to be of commercial value.

As penicillin production increases, more and more of the 'natural' penicillin will be purified, and the white substance—which is already in use—will eventually replace the yellow product.

Treatment

The results of penicillin therapy have been so widely published that little further comment is necessary. Suffice it to say that Professor Fleming's ambition was fully realized by the drug he discovered: the anti-bacterial properties of penicillin have no equal in the treatment of war wounds.

The wonder drug has practically all the advantages of the sulphonamides and none of the disadvantages. It is deadly to streptococci and staphylococci and the germs of the common forms of pneumonia and meningitis. It is equally effective in the treatment of infections of the skin, such as secondarily infected eczema and impetigo, and is the most powerful weapon yet produced in the fight against venereal disease. Most important of all, its toxic effects are slight. As Dr Florey said, it is the one drug that gives no cause for worry about overdose.

Penicillin is prepared in the form of a sodium or calcium salt, and the most general way of administration is by injection. When the drug reaches the blood-stream it mixes with the blood and is pumped round the body by the heart. Sooner or later, of course, it meets the kidneys, whose function is to remove waste materials from the body. Penicillin is not a substance naturally found in the body, and it is, therefore, treated as waste material, and excreted as rapidly as possible. To quote Professor Florey again, "It is like pouring water down a basin with the plug

out." To maintain continually an effective level in the blood, therefore, injections had to be repeated very frequently day and night. Later, however, it was found possible, by giving larger doses (such as 500,000 instead of 100,000 units) and thus producing very high concentrations in the blood, to treat diseases satisfactorily without having to maintain the blood-level by continual injections. In addition, a preparation is now available in which the penicillin is given in beeswax intramuscularly, the effect being to prolong the action to such an extent that one injection daily can suffice; this is because by this means the penicillin is absorbed slowly from the area of injection, so that a constant concentration is maintained.

Other forms in which the drug is prepared include dusting-powders, ointments, lozenges, and eye ointments. Professor Fleming has predicted that when the supply problem is solved it is conceivable that we might have penicillin tooth-paste, penicillin face-powder—and even penicillin lipstick! Taking the drug by swallowing has so far proved comparatively unsuccessful, as it is inactivated by hydrochloric acid in the stomach and bacteria in the intestines. However, attempts are already being made to overcome these difficulties.

Like the sulpha drugs, the lower concentration of penicillin is *bacteriostatic*—that is, it prevents the bacteria from multiplying, and enables the body defence mechanism to destroy the invaders. It is this action which was relied upon for earlier methods of treatment. It is now known that any higher concentration of penicillin is intensely *bactericidal*—which means that it kills germs in a very short time. This lethal action is used in the newer forms of treatment.

Penicillin is not a cure-all. So wide a publicity has it received that in some quarters the belief has sprung up that it can conquer every form of disease. It must be said, therefore, that it has no power over the tubercle bacillus, to mention one disease, nor can it cure a number of commoner infectious diseases such as measles, chicken-pox, influenza.

After penicillin had been in general therapeutic use for a little while it was found that certain infections which had

PENICILLIUM NOTATUM, THE FAMOUS MOULD

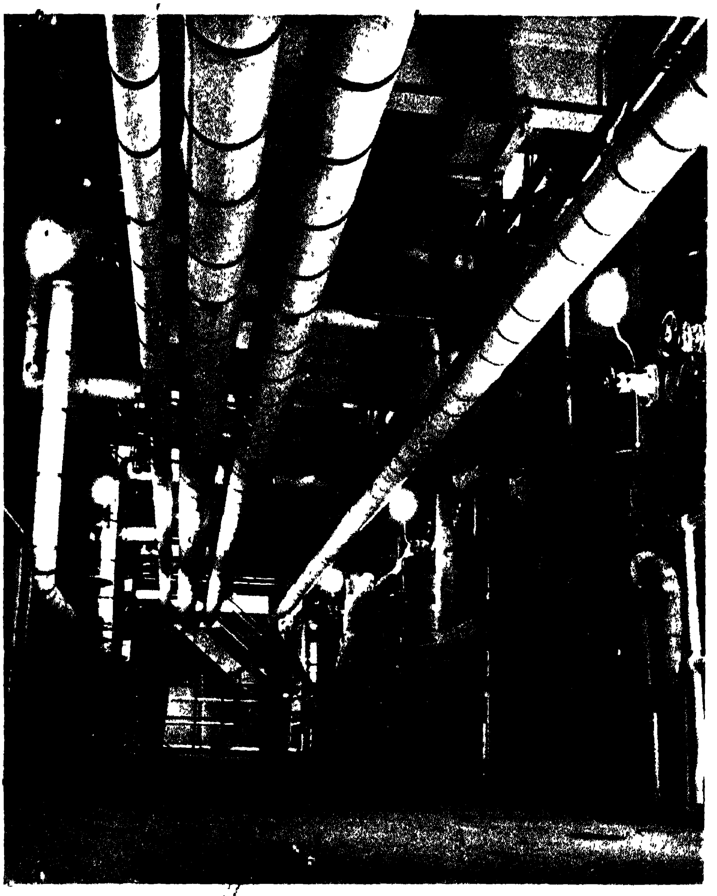
The mould is growing in surface culture in one of the flasks specially designed for penicillin production. The dark portion is the liquid from which the mould derives its nourishment

By courtesy of Glaxo Laboratories Ltd

SURFACE CULTURE OF PENICILLIN

Part of the incubator used for maintaining the mould at a constant temperature during the period of growth when the penicillin is formed

By courtesy of Glaxo Laboratories, Ltd



PENICILLIN PRODUCTION AT BARNARD CASTLE

A small portion of the elaborate plant required for the deep-culture method of producing penicillin

By courtesy of Glaxo Laboratories, Ltd

originally responded to the drug were becoming much less susceptible to this treatment. The reason for this was that certain organisms had acquired a resistance to penicillin. The publication of these facts was attended by some popular exaggeration; and it must be stressed that in spite of this unwelcome development, penicillin is still the most powerful therapeutic weapon in the armoury of the medical profession.

Recognition

For their wonderful work both Professors Fleming and Florey received well-deserved knighthoods. Then, in 1945, the Nobel Prize for Medicine was awarded jointly to the Big Three of penicillin—Fleming, Florey, and Chain.

Not all the members of the Oxford team could share in these prizes, but happily their leaders have lost no time reminding the public of the services they rendered. The story of penicillin is one of superb co-operation, unmarred by any petty jealousies or rivalries. Nor was this spirit confined to the scientists; it infected manufacturing chemists, traditional competitors, who willingly pooled their knowledge and resources for the common cause.

It was this harmony that made possible the production of penicillin when it was so sorely needed. The happiest feature of the story is that the wonder drug came in time to save the lives of those who most deserved it—soldiers wounded on the battlefield.

The Aftermath: Streptomycin

The discovery of penicillin had two important results: one was to provide medical scientists with a new field for research, and thereby stimulate their efforts; the other was to stimulate a number of over-zealous but under-informed journalists to unleash wild reports of 'sensational' new discoveries, with the suggestion that man's fight against disease was nearing its triumphant conclusion. And of the 'successors' to penicillin none has received more publicity than the drug known as streptomycin.

Streptomycin is an antibiotic obtained from a micro-organism called *Streptomyces griseus*, whose place in the family of living things is between the bacteria and the fungi. It was discovered in 1944 by the American Dr S. A. Waksman, working in collaboration with Schatz and Bugie. The early laboratory reports on it were startling. It destroyed the terrible tuberculosis bacillus both in the test-tube and in infected mice. Medical scientists, remembering the premature claims advanced on behalf of Koch's tuberculin and other alleged cures for tuberculosis, were cautious. But certain sections of the Press, especially in the U.S.A., were irresponsibly optimistic, and the hopes of thousands of sufferers were unjustly raised; for the results of the first investigations made at the Mayo Clinic were much less encouraging.

Many series of tests with streptomycin have now been made, in the United Kingdom as well as in America; but it is still too early for its true clinical value to be assessed. The most promising results so far have been obtained in the treatment not of pulmonary or bone tuberculosis but of the deadly disease of tubercular meningitis. In this country tests have been carried out by the Medical Research Council at selected hospitals in London, Liverpool, and Glasgow; and the first reports confirm that the drug has certainly proved more effective than any other known form of treatment for this disease.

This does not necessarily mean that streptomycin is a complete 'cure' for tubercular meningitis. This disease, which occurs most commonly among children, claims an average of about 1800 new cases a year in this country. That sounds a small figure; but the annual mortality rate is a very big figure—100 per cent. Whether or not streptomycin will reduce this figure cannot yet be said. Only time will show if it produces any permanent cures. But in some of the cases treated already it has undoubtedly prolonged life and relieved symptoms to a hitherto undreamed-of extent. The Medical Research Council reports suggest also—but in very guarded terms—that streptomycin may prove effective against certain types of lung tuberculosis as well as tubercular meningitis.

Streptomycin has proved efficacious also in the treatment of infections of the urinary tract which do not respond to penicillin therapy.

For some time after its discovery streptomycin was available in Britain in only very small quantities, all supplies having to be obtained from America. Now, however, following the reports of the Medical Research Council, it is being manufactured in England on a rapidly increasing scale.

But streptomycin is still on trial. Medical science has suffered too many setbacks and disappointments, especially in its fight against tubercular infections, to accept a new ally until its worth has been proved beyond all reasonable doubt. Professional conservatism has frequently obstructed progress; but it has also ensured the preservation of a high standard of practice that would probably not have been maintained in its absence.

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